

**FOREIGN GOVERNMENT PHARMACEUTICAL
PRICE AND ACCESS CONTROLS**

**Submission by the Pharmaceutical Research and Manufacturers of America
(PhRMA) to the Department of Commerce**

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Foreign Government Pharmaceutical Price and Access Controls

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I. Introduction and Executive Summary of this Submission

The Pharmaceutical Research and Manufacturers of America (PhRMA) appreciate this opportunity to submit these comments regarding foreign government price and access controls on pharmaceuticals to the Department of Commerce in response to the Federal Register notice (69 Fed. Reg. 30882) dated June 1, 2004, requesting such information.

Foreign government price and access controls on pharmaceuticals are the single most important trade barrier facing innovative U.S. pharmaceutical companies in developed country markets around the world. Such controls are pervasive outside the United States, and have significant deleterious effects not only on the U.S. industry, but more importantly on U.S. patients and the U.S. economy as a whole. Moreover, these interventionist measures have very serious ramifications for foreign patients and global levels of research and development, and result in misallocated health care dollars.

This Submission is intended to provide U.S. policy makers with an overview of the types of government price and access controls that characterize overseas developed country markets for U.S. pharmaceuticals, and substantial analytical material regarding the effects of those measures – both in the United States and abroad. It proceeds in several parts.

The mechanisms used by foreign governments to control supply and demand in their pharmaceutical markets are varied and complex. To understand the true ramifications of these systems, however, an appreciation of this variety and complexity is crucial. Also crucial is an understanding of the manner in which seemingly neutral mechanisms are regularly implemented so as to compound the burden to the pharmaceutical industry and discriminate against innovative products. For this reason, a substantial section of this Submission and its Annexes are devoted to providing resource material on these issues. In Section II, we review common types of price and access control mechanisms and provide examples of countries that have used them in recent years. Annexes A and B of the Submission then provide more detailed information, country-by-country, for every country in the Organization of Economic Cooperation and Development (OECD).

For purposes of comparison, Section III of this Submission provides an overview of the salient characteristics of the U.S. pharmaceuticals market. It describes the importance of large Pharmaceuticals Benefits Managers (PBMs), the importance of generic competition, and the key features of U.S. federal programs that seek to provide medicines to certain discrete populations. The important distinguishing feature of the U.S. market from the regimes detailed in Section II can be summarized in one word: competition. Private sector organizations use market forces and competition to control costs and promote efficiencies in pharmaceutical consumption. The only exceptions are certain federal programs described in this Section, but these affect just a small percentage of the overall U.S. market.

One of the most important negative effects of foreign price controls is on future innovation. This effect is perhaps the most important because it compromises the health of future generations of American patients. Section IV of this Submission provides background material on innovation in the pharmaceutical industry. The costs of developing a new drug have increased dramatically over the past decade, and today exceed \$800 million dollars. Yet the fruits of this massive investment are in some ways priceless. The past decade has seen enormous advances in drug therapies for scourges such as rheumatoid arthritis (RA), HIV/AIDS, Parkinson's disease, Alzheimer's disease, schizophrenia, diabetes, high blood pressure and high blood cholesterol - resulting in patients living longer, more productive lives both in the United States and around the world. Between 1993 and 2003, Americans obtained more than 363 new medicines, biologics, and vaccines approved by the U.S. Food and Drug Administration to prevent or treat more than 150 diseases and conditions. The fruits of this innovation benefit millions of patients each year. Yet innovation in the pharmaceutical industry is poorly understood by the public and subject to a number of misconceptions. For this reason, we have addressed some of the most common of these issues in Section IV as well, including the health care and financial benefits of having multiple drugs in a therapeutic class, the relationship and relative productivity of public vs. private research and development in the United States, and the relative magnitude of pharmaceutical industry promotional expenses as compared to investment in research and development.

Section V of this Submission then describes in detail the effects of foreign price and access controls. First, in response to Commerce's specific request in the Federal Register notice, we have described how foreign price and access controls operate to discriminate against innovative products and reduce trade in pharmaceuticals. These government interventionist measures function in a manner completely analogous to traditional non-tariff barriers about which U.S. trade agencies have been concerned for decades.

This Section then describes the ramifications of foreign price controls on U.S. patients and patients abroad. Chief among these effects is a decline in the number of innovative new drugs produced. A July 1, 2004 study by the Boston Consulting Group quantified this effect, and found that foreign price controls result in 10 to 13 fewer drugs being developed every single year. Over a decade, this implies that between 100 and 140 new drugs would be foregone. In addition to affecting the health of patients waiting for new cures, these "missing" new drugs have another important effect – on U.S. prices. On the basis of a review of the empirical third-party economic literature and accepted economic theory, the BCG study concludes that eliminating foreign price controls would result in lower U.S. prices. This "competition effect" is due to fact that new entrants in a drug class generally (according to the literature and economic theory) result in lower prices.

Foreign price and access controls have even more severe effects on patients abroad, and this is part of the reason why it is in the interest of foreign governments to re-orient their policies toward market-based alternatives. Foreign patients suffer from

reduced access to innovative drugs as a result of lengthy government delays in the reimbursement bureaucracy and from diminished health outcomes

Finally, government price and access controls on pharmaceuticals impose significant economic consequences on the United States in the form of higher health care costs and fewer jobs. After an extensive analysis, the BCG study found that if foreign price controls on pharmaceuticals were eliminated, approximately 90,000 – 105,000 new jobs would be created in the United States. For Europe and other price controlled markets, the economic consequences are even more severe, and come in the form of a scientific brain drain, higher health care costs and the overall decline of their innovative pharmaceutical industry. Another “side effect” of these measures is to distort competition in the generic pharmaceuticals market. In many foreign markets, the prices of generic drugs exceed the prices of such drugs in the United States. In some instances, this is the result of deliberate discrimination in favor of local producers. In others, it simply reflects the fact that the prices of innovative pharmaceuticals are set so low, there is little incentive for generic producers to enter the market and compete vigorously on the basis of price. Either way, the result is misallocated health care resources – in colloquial terms, a penny-wise and pound-foolish policy. Innovative pharmaceuticals are squeezed and governments overpay for simple copies.

The research-based pharmaceutical industry has worked for years to advocate for reform to these government policies that discourage innovation and reward imitation. Section VI of this Submission details some of the litigation tactics employed to address price controls measures in Europe that violated EU law. Unfortunately, outside the courtroom, due to the political sensitivity of health-related issues, the advocacy efforts of the industry have often been frustrated. The effects of these measures on U.S. consumers, U.S. industry and the U.S. economy, however, can no longer be ignored by U.S. policymakers. The attention and efforts of U.S. trade agencies is crucial to progress in promoting an international policy environment friendly to innovation in this sector.

II. Overview of Foreign Government Pharmaceutical Price and Access Controls

Government-imposed pharmaceutical price controls and other access barriers to innovative pharmaceuticals are pervasive outside the United States. These measures tend to be non-transparent and highly complex, and also vary substantially from country to country.

The prevalence outside the United States of such market intervention mechanisms is likely related to the fact that governments in most other countries provide some kind of national health insurance that covers the vast majority of the population. Such governments dominate the health care “marketplace,” and effectively operate as monopsonistic purchasers of pharmaceutical products. Many governments abuse this near-total control of the local health care market to obtain innovative drugs at prices significantly below what they would cost in a free market, and avoid paying for the research and development (R&D) costs of discovering and developing these important and innovative medicines.

The trade-restricting and trade-distorting measures imposed by foreign governments often share several characteristics. Typically, they are motivated by the government's desire for short-term (typically one-year) health care cost containment, *not* therapeutic considerations. They often systematically ignore the therapeutic benefit or value of newer, innovative medicines, focusing instead only on their short-term cost. In fact, such policies are usually established in the context of "silo" budgeting – the government's pharmaceutical budget is considered in isolation, ignoring the savings in other parts of the health care system, such as reduced hospitalizations, that can result from the use of better and more innovative medicines. Through sometimes subtle and other times less subtle measures, these government systems also generally aim to influence the prescribing decisions of doctors in a manner based on economic, rather than medical or therapeutic, considerations. Finally, many price and access control mechanisms imposed on pharmaceutical sales outside of the United States have the effect of creating hurdles for innovative pharmaceutical products that are not faced by other types of medical treatment, such as the need to demonstrate "cost effectiveness." As the majority of medical advances in innovative medicines are funded and occur in the United States, these practices have a disproportionate effect on this crucial U.S. industry, and tend to favor less innovative, but more often locally-based, producers of generic medicines.

To understand fully how a country's health care system systematically undervalues or impedes access to new medicines, it is important to understand in detail how that system operates, and the various bureaucratic processes that relate to the reimbursement of medicines, as well as to the valuation of health care generally. Systems that superficially seem fair and objective can often be much less transparent than they appear, and much more discriminatory against innovative medicines than they claim.

The country summaries attached at Annex A provide a brief description of how key foreign governments value and reimburse new medicines. These summaries provide an initial overview of the ways in which foreign governments delay or deny access, or fail to recognize fully the value of new medicines. The slides attached at Annex B also provide additional factual information on the price controls used by governments in seven key markets (the UK, Germany, France, Japan, Canada, Poland, and Spain). The Annex B slides also provide illustrative examples of market interventions in every other OECD country outside the United States. While these later slides are not exhaustive in listing all the price and access controls imposed by these other OECD governments, they provide useful background regarding the magnitude of the problem.

As is apparent from the country-specific analyses provided in these Annexes, there are a number of common mechanisms that governments employ to restrict the supply of pharmaceuticals to artificially low levels or to depress patient and doctor demand for the latest products. Some countries rely on government-set ceiling prices, while others demand regular, large "rebates" from pharmaceutical manufacturers. Still others use profit controls, volume restrictions, or highly-restrictive formularies. Some

countries even fine doctors if they prescribe “too many” innovative medicines for their patients in a given month. All of these mechanisms distort market-based trade.

A. Role of Government-Set Reimbursement Prices in Establishing Market Prices in Foreign Countries

To fully appreciate the effect of foreign price and access controls imposed through government-dominated health care systems, it is important to recognize that in these systems, the reimbursement price determined by a government authority often effectively functions as the market price for an innovative medicine. The reasons for this phenomenon are varied and differ somewhat by country. One common reason is the absence of any mechanism for pharmaceutical manufacturers to provide information directly to patients in these countries. In every major market outside the United States, the entities that know the most about the science behind a new drug – the inventors and manufacturers of that drug – are prohibited by law from communicating directly with patients to make them aware of their treatment options. This is true even with respect to the internet. Every OECD country (except New Zealand) prohibits pharmaceutical manufacturers from providing such information on a website accessible to patients seeking health information.

Cultural factors also account for the fact that the reimbursement status of medicines as well as their price determine their availability and price in the marketplace. Particularly in countries where the tradition of government-provision of health services is strong (*i.e.*, patients are accustomed to getting health care for “free”), the ability of private companies to create a private market on their own is exceedingly limited. In many countries, there is entrenched social opposition to the notion that patients should contribute at all to their own health care costs and to the notion that contributions to health care costs should be based in any way on progressive “ability to pay” or income considerations.

A final factor inhibiting the development of private markets in many OECD countries is the absence of meaningful pharmaceutical coverage in private health insurance plans (as a result of government intervention). Australia is not unusual, for example, in establishing policies that strongly discourage private health insurers from offering pharmaceutical coverage in competition with the government Pharmaceutical Benefits Scheme.

For all of these reasons, pharmaceutical companies are critically dependent on the level of reimbursement established by government health authorities for their products in foreign countries. Such prices effectively function as government-set market prices, with little realistic opportunity for manufacturers to develop a private market to provide their products to consumers willing to pay market-based prices reflecting the value of innovative medicines.

B. Glossary of Common Types of Government Intervention Strategies

Some of the more common forms of market-distorting intervention are:

- “International” Reference Pricing – The government assigns prices to new products in reference to some basket of prices for that product in other markets. This typically has the effect of importing and magnifying the price control policies of other markets. These regimes differ in their severity, depending of the reference countries chosen and whether the reference price used as a benchmark is an average, some kind of weighted average, or the lowest of the prices in the reference markets.

Examples: *Belgium* limits the price of medicines at 10%-15% below the European average. *Canada’s* PMPRB determines maximum allowable prices by reference to a basket of prices in seven countries (France, Germany, Italy, Sweden, Switzerland, United Kingdom and United States FSS price). The price considered non-excessive by the PMPRB must be at or below the median of the prices in these countries. *Brazil* recently issued a price control decree that establishes local prices at the level of the lowest price at which the medicine is sold in any of certain selected countries.

- “Therapeutic Class” Reference Pricing: Prices for new products are referenced to older, and often, off-patent products in the same “therapeutic class” (e.g., hypertension). Such policies not only systematically fail to recognize the therapeutic advances that new products represent, but are exacerbated by the fact that the older “comparator” drugs themselves have been systematically devalued by successive price cuts.

Examples: *Japan* can use comparators as much as 20 years old (which would have been devalued by 10 successive biennial price reductions) in establishing the prices of new drugs. *Australia* has established several therapeutic categories where prices for all products in the class are referenced to the price of an old, low-cost generic product. The *Netherlands* establishes therapeutic product “clusters” containing old and newer products; the maximum reimbursement price is the average of the cluster, which systematically rewards older, cheaper products and punishes newer, more innovative products. The province of *British Columbia* in *Canada* decrees that the price of one product in a therapeutic class will act as the “reference price.” The public plan will then reimburse all products in that class at the same level as the reference price, regardless of whether another medicine is newer or more appropriate for a particular patient.

- Profit controls: Arbitrary limits are set on profits which companies may make per product, or in total, for a given period of time. If a company exceeds these limits, it may be required to compensate the government for the “excess” profit, or accept a price cut. The policy has the effect of establishing a ceiling return on investment (which, in practice, can be entirely non-transparent), undermining incentives for research.

Example: The *United Kingdom* places limits on the profit that a company may make on its sales to the NHS. *Spain* sets profit margins for products as a percentage of “allowable costs.”

- Doctor budgets: Individual doctors are assigned a set “budget” for a given period, from which to administer treatment. If they exceed this budget, they will be financially penalized or fined by the government. The budget system forces doctors to focus on the short term costs of treatments (and hence, to under-prescribe drugs deemed too “expensive”) rather than focus on the therapeutic benefits.
- *Examples:* *Germany* has employed such a system in the past. The *Czech Republic* is currently administering such a system. In *Korea*, the government also discourages prescription of innovative medicines by evaluating providers based on the proportion of prescriptions they write for so-called “expensive drugs.”
- Direct Price Controls: Some governments, notably *Canada*, establish maximum allowable prices that pharmaceutical manufacturers are allowed to charge for their product (regardless of the reimbursement status of the product). Any attempt to impose higher prices in the marketplace can result in serious fines for the manufacturer.

Other governments use direct price controls to control the reimbursement price that products may receive pursuant to the national health care system. Given that the private pharmaceutical market in most developed foreign countries is extremely small and that opportunities to grow this market are limited by the government, the effect of government ceilings on reimbursement prices are to establish direct ceilings on market prices as well. Governments impose these direct price controls through a variety of mechanisms including setting initial reimbursement prices upon launch of a new drug, and/or regularly cutting the prices of drugs already on the market either on a case-by-case basis or across-the-board.

Examples: Canada uses both types of direct price controls. The Patented Medicines Prices Review Board is charged under Canadian law with regulating the prices of patented (but not generic) medicines to ensure that they are not “excessive.” Then, in addition, Canadian provinces establish maximum reimbursement prices that are typically significantly lower than the allowable ceilings established by the PMPRB. The provincial governments have also resorted with frequency to price freezes to prevent even inflation adjustments in the reimbursement prices established by the provincial governments. Since many provinces will not pay a higher price than the lowest available price anywhere in the country, the price freeze actually applies to more provinces than the one that originally implemented it. For example, Ontario has had a price freeze for over 10 years.

As another major example, *Japan* institutes biennial price cuts of existing drugs. This every-other-year review process is well-established in Japan and for the past twenty years has resulted without exception in the Japanese government cutting substantially the maximum allowable reimbursement rates for innovative medicines.

In *Italy*, the government has similarly resorted in frequent across-the-board price cuts in the reimbursement prices of innovative products. Unlike in Japan, however, these cuts have been announced in an *ad hoc* fashion, with little meaningful consultation with industry, and no regard for the importance of business planning or stability in the marketplace. Since June of 2001, the Government of Italy has imposed seven different measures that have had a severe impact on the price of reimbursable drugs. The latest of these decrees, adopted in June 2004, imposes a 6.8% reduction in the ex-factory price of reimbursable drugs. This latest measure is expected to cost the pharmaceutical industry 495 million euro.

- Volume Limitations: The government may mandate an absolute maximum volume of a new drug that may be sold, or very often, tie a new drug's reimbursement price to a set volume ("a price-volume" agreement). This form of government mandated rationing often can have the effect of hurting the most promising new drugs (for which demand will be great) the most.

Examples: *Australia* often links the reimbursement price of a new drug to a set volume. Once that volume is exceeded, the price falls (the alternative is to take it off the market), disproportionately damaging promising or popular new treatments in the marketplace as opposed to rewarding them. *France* also "negotiates" price-volume agreements with manufacturers of new medicines, and requires price reductions or cash payments to the Government if a manufacturer exceeds the set volume limits.

- Rebate Requirements: The government may require a pharmaceutical manufacturer to pay back a set percentage of its sales as a "rebate" to the payer agency. Many governments impose such rebate requirements in an *ad hoc* fashion, to cover unexpected budget shortfalls in a given year.

Example: In 2004, *Germany* has imposed a 16% mandatory rebate on the sales of innovative products; the rebate does not apply to sales of generic products. The 2004 mandatory rebate follows a 6% rebate in 2003, and an allegedly "one time" lump sum payment imposed by the Government on innovative companies in 2002. *Italy* too is in the process of implementing a highly problematic mandatory rebate scheme in 2004. The most recently passed Italian legislation on this point provides that pharmaceutical manufacturers are liable to payback to the Italian state 60% of the amount of any "overspending" by Italian regional authorities on their health budget for pharmaceuticals. Other key players whose

fees are encompassed by these budgets, however, such as local pharmacists and wholesalers, are exempted from the rebate obligations.

- Reimbursement Restrictions: Governments may decide to reimburse use of the drug only under circumstances that are much narrower than those for which the drug is medically approved by regulators. Governments can thus essentially usurp the role of the physician in determining which drug is appropriate. These measures are another form of rationing of innovative medicines.

Examples: Australia limits the reimbursement for a number of new, innovative medicines to uses much narrower than those approved by the Australian regulatory agency. For example, the important antibiotic Zithromax, approved in Australia for the treatment of a wide variety of infections, is approved for reimbursement by the PBS only for the treatment of Chlamydia. And Fosamax, an important osteoporosis medication that can actually prevent the onset of the disease, is reimbursed in Australia only *after* a patient has broken a bone.

Restrictive conditions on reimbursement have also been a major problem in *Korea*, where the government has strictly limited the reimbursement of new medicines through a non-transparent and non-science based process.

- “Fourth Hurdle” Requirements / Cost-Effectiveness Reviews: Governments are increasingly considering factors other than safety, efficacy and quality in approving new drugs for marketing or reimbursement. Such a fourth hurdle effectively takes decision making out of the hands of health care providers, and subjects access decisions to determinations such as “cost effectiveness” or other “socioeconomic criteria.” Unlike the science-based processes which determine whether a drug is safe, effective and of high-quality, such factors are typically non-transparent, non-scientific, and arbitrary.

Examples: Australia’s system of pharmacoeconomic “cost effectiveness” analysis purports to be objective and scientific, but in practice is often non-transparent, fails to factor in significant benefits (and thus, not rigorously scientific), and can serve as a disguised form of cost-containment. *New Zealand’s* PHARMAC applies an even more rigid form of cost effectiveness analysis which has resulted in very few new drugs being listed for reimbursement at all in recent years.

- Parallel Trade: Parallel trade is a legal practice in the European Union (EU) and involves a supplier who buys drugs in low-cost member states, often in Southern Europe, and sells them at a discount in countries where prices for that product are higher, often in Northern Europe. In some European countries, governments have even imposed parallel trade “quotas” on pharmacists, who are obligated to sell at least 10% parallel traded products. The essential purpose of this practice is arbitrage between countries with different prices. Studies have demonstrated, however, that the parallel trade practice has had little impact on prescription drug prices. For example, in the U.K., one of the largest importing countries, prices

have dropped by less than two percent. In Sweden, the average price fell by just 4 percent.¹ One important recent study also confirmed that the small savings from parallel traded products do not even go to consumers. This 2004 study by an economist at the London School of Economics found that 86% of the price difference is gained by parallel importers, 13% is gained by payors, and 1% is gained by pharmacists, with nothing left for consumers.²

III. The U.S. Market-Based System of Health Care and Cost-Containment

By contrast to many of the OECD countries, the prices for innovative and generic medicines in the United States are determined by market forces. With the exception of discrete populations where medicines are provided by public entities, private sector organizations use market forces and competition to control costs and promote efficiencies in pharmaceutical consumption in the United States. Only 2% of the U.S. market is subject to direct controls on prices, with an additional 12% subject to mandated rebates.

A. Private Sector Competition: PBMs, Managed Care Organizations and other Intermediaries

The U.S. market is characterized by intermediary purchasers of pharmaceuticals including managed care organization, insurers, and Pharmaceutical Benefits Managers (PBMs). These entities either directly or by contract purchase pharmaceuticals or negotiate for the purchase of pharmaceuticals on behalf of the members of health plans including public and private sector employers.

These entities aggregate together drug consumers,³ and then use their ability to influence the choice of medicines by prescribers and patients to obtain discounted prices from drug makers and discounted prices from the pharmacies that dispense medications. These entities use strategies that include the use of formularies (lists of covered and preferred medicines), differential cost sharing (including tiered copayments), prescriber and patient education, and therapy management protocols (such as step therapy) to influence the selection of a medicine by a prescriber. They can undertake this strategy because they maintain that, for many patients, several different medicines may provide patients with similar medical benefits.

These entities employ strategies that may seem superficially similar to those strategies outlined in the previous section of this Submission to reduce spending on

¹ “E.U. Parallel Drug Trade Cited in U.S. Reimportation Debate,” *Drug Industry Daily*, 12 November 2003.

² P. Kanavos et al., “The Economic Impact of Pharmaceutical Parallel Trade in European Union Member States: A Stakeholder Perspective,” London School of Economics and Political Science (London, England: London School of Economics and Political Science, January 2004).

³ Last year AdvancePCS covered 75 million individuals, Medco Health Solutions 65 million and Express Scripts 57 million - each more than the entire Medicare population. In addition, the next three largest PBMs had enrollments of 32 million, 24 million and 11 million individuals.

pharmaceuticals. However, the key distinction with what happens in foreign countries, is that these entities employ these tools in a market context. First, U.S. consumers and those who pay for medical care (including employers), including pharmaceutical care, have choices among health plan providers. If they are not pleased with the services they receive or the prices they are paying, they have the ability to choose a different provider. This market dynamic is not available to most foreign consumers who live in pricecontrolled markets.

Second, pharmaceutical makers have a choice. They may reach a pricing agreement with one entity and not another. No purchaser exercises the monopsonistic power discussed in the previous section that makes the purchaser a price setter and not a price negotiator.

Intermediary purchasers of pharmaceuticals including managed care organizations, insurers, and PBMs have demonstrated through their success in the competitive private market that they add substantial value for customers and patients in the health care system. That value takes the form not only of reduced spending on pharmaceuticals, but also better management of the use of prescription drugs to achieve improved patient outcomes and constrain overall health system costs.

The creation and growth of these intermediary purchasers of pharmaceuticals is an example of the genius of the decentralized, private market in health care. In essence, the private market 'invented' mechanisms to increase health system efficiency and as a mechanism for balancing conflicting incentives within the pharmaceutical marketplace. By acting as advocates for patients and payers, these intermediaries exert countervailing pressure on drug makers and doctors to achieve a balanced approach that seeks optimum quality at optimum cost for a complicated set of services and products about which the average consumer has little expertise other than being able to obtain prescriptions easily when they are needed.

To be sure, these intermediaries can seek to overemphasize cost considerations to the detriment of benefit considerations. However, to the extent that these intermediaries function as an integral component of comprehensive health plans responsible for the total cost of patient care, and particularly to the extent that consumers are free to choose the health plan and/or PBM in which they have the greatest confidence, the competitive marketplace will also check this temptation to overemphasize cost. Additionally, many health plans ensure their employees have appeals processes in place to ensure patients are protected for an overemphasis on cost considerations. Thus, through its complex system of natural checks and balances, the private market is able to obtain the desired outcome of the most clinically appropriate care for the individual patient at the best price.

The recent Medicare debate on Capitol Hill regarding coverage of prescription drugs focused significant attention on the cost-saving potential of these intermediaries including PBMs. The non-partisan Congressional Budget Office (CBO) has found that multiple competing private-sector plans can contain costs more effectively than a government-controlled benefit. The CBO has scored the 2003 Medicare Modernization

Act as getting a higher "cost management factor" than non-private sector bills-which CBO defines as the effect of price discounts, rebates, utilization controls, and other tools that a private plan might use to control spending for Medicare. CBO has repeatedly assigned higher cost management factors to bills that rely on multiple plans negotiating savings than those that rely more heavily on the participation of the federal government. Put simply, the most efficient way to manage pharmaceutical spending is through market mechanisms, not through empowerment of government bureaucrats.

B. Private Sector Competition: Aggressive Generic Competitors

The United States, in contrast to most other OECD countries, maintains a highly-efficient generic market with relatively low generic prices. In the United States, generic drugs are 30% to 80% less expensive than their brand-name counterparts.⁴ The CBO has estimated that the ability to substitute generic for branded drugs saved U.S. consumers between \$8-10 billion in 1994, and reduced the current discounted value of the returns of marketing an innovative drug by 12%.⁵ In 1984, the year the Hatch-Waxman Act was passed, only 19% of drugs sold in the United States were generics; by 2001, the generic share had increased to 45% and it is projected to be 57% by 2005.⁶ The situation is far different in most other OECD countries, where (as described in more detail in Section V.C.2, below) generic drug prices are often higher than in the United States.

C. Federal Supply Schedule

The U.S. government does employ price-controls for small, discreet elements of the population. The Federal Supply Schedule (FSS) is a schedule of contracts and prices for frequently-used services and supplies, including pharmaceuticals, available for purchase by federal agencies and other limited entities.

FSS pharmaceutical prices charged to the Veterans Administration (and certain other federal agencies including the Department of Defense, Public Health Service and Coast Guard) are capped by statute. Prices for innovator drugs sold to these four agencies are capped by law at a "Federal Ceiling Price" substantially below market price. The Federal Ceiling Price (FCP) is 76% of the average *market based* price, called the Non-Federal Average Manufacturer Price (Non-FAMP). This basically amounts to the average net price paid by wholesalers minus an "additional discount" of at least 24%. In other words, FCP is 24% or more below the average price paid by wholesalers- *a price that already includes market discounts*. If a manufacturer does not "agree" to price caps, its drugs are excluded by law from reimbursement by the Medicaid program throughout the country, plus several other Government programs. VA prices are the result of statutory price controls, and not a negotiating process

⁴ See, e.g., S. Kreimer, "Prozac's Progeny; With Eli Lilly's Patent Expired, Consumers and Competitors Hope to Benefit from Generic Formula of Blockbuster Drug," *The Houston Chronicle*, 4 November 2001.

⁵ CBO, "How Increased Competition From Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry, July 1998

⁶ 2005 forecast based on a regression line by National Economic Research Associates.

These U.S. price controls are different in effect, however, from the price controls employed by most other developed country governments in that they apply to a very small portion of the population and a small percentage of U.S. sales. They do not displace the private market in the United States. Sales to the VA, Department of Defense, Public Health Service and the Coast Guard are roughly 2% of total pharmaceutical sales. By contrast, for example, the Australian Pharmaceutical Benefits Scheme represents 96% of the market in Australia. The ability of pharmaceutical companies to operate in the two markets is simply not comparable.

D. Medicaid

Medicaid, a Federal-state partnership that serves as the nation's principal public health-care program for low-income individuals, provides outpatient prescription drug coverage in all 50 states. While this program relies to an extent on government-directed price control measures, the program accounts for a small proportion of the U.S. market and also takes into account market forces in important ways.

The federal government and the states share funding for the program. The federal share of Medicaid expenditures averages about 57 percent. The states administer the program under broad federal guidelines that allow each state to determine, within established limits, exactly who is covered, the extent of services offered, and the method of reimbursing providers. All states offer outpatient prescription drug coverage to most of their Medicaid beneficiaries, though they are not required to do so.

Pharmaceutical companies are required by federal law to provide rebates on their products to Medicaid and other government programs. In return, state Medicaid programs must cover all prescription drugs manufactured by a company that has entered into a rebate agreement. There are two components of the rebate amount for single source and innovator multiple-source drugs: 1) The basic rebate – which is either 15.1 percent of the average price the manufacturer charges the retail pharmacy class of trade (AMP), or, if greater, the difference between the AMP and the best price offered to the private sector, plus 2) a price inflation rebate, which is equal to the full amount by which the manufacturer's AMP increases since 1990 exceed the rate of increase in inflation. In 2001, manufacturers returned an estimated \$4.7 billion in rebates to the federal government and states—in effect an extra business tax.⁷ Since 1991, brand manufacturers have paid approximately \$28.8 billion in Medicaid rebates.⁸ In addition to these rebates, some states also extracted supplemental rebates from manufacturers. Under the federal Medicaid law, if the state establishes a formulary all drugs of manufacturers who participate in Medicaid by offering federally-required rebates must be made available to Medicaid beneficiaries in that state unless the drugs are excluded for clinical reasons. These programs restrict Medicaid beneficiaries' access to prescription drugs

⁷ HCFA-64 data reporting system 2000-2001, <<http://cms.hhs.gov/medicaid/mbes/ofs-64.asp>> (January 2003).

⁸ HCFA-64 data reporting system 2000-2001., <<http://cms.hhs.gov/medicaid/mbes/ofs-64.asp>> (January 2003).

unless the manufacturer pays the state additional rebates far beyond the significant rebates required by federal law.

A 1996 CBO report examining the impact of the Medicaid rebate on prescription drug pricing found that while the basic Medicaid rebate has lowered Medicaid's expenditures on outpatient prescription drugs, spending on prescription drugs by non-Medicaid patients may have increased as a result of the Medicaid rebate program. Earlier and later GAO studies report similar effects. These studies show the unintended consequences price controls have even on a limited basis in the U.S. market. Notwithstanding these effects, however, and even taken together with the FSS restrictions described above, these federal programs still do not approach the effect of most foreign government interventions in the marketplace outside the United States.

IV. Background on Innovation in the Pharmaceutical Industry

The pharmaceutical industry is a major driver of growth in the U.S. high-technology economy. In 2003, members of PhRMA spent an estimated \$33.2 billion on pharmaceutical R&D. The new medicines resulting from innovation offer increasingly better treatments and health care options for patients.

As will be detailed in Section V of this submission, one of the most pernicious effects of foreign price controls is on the level of innovation in the pharmaceutical industry. For this reason, this section provides additional background on innovation in the industry and addresses some common misperceptions regarding pharmaceutical innovation. The sub-sections below address the cost of innovation in the pharmaceutical industry, the rate of investment in pharmaceutical R&D, and the main determinants of R&D – in other words, how much pharmaceutical companies invest in research and development and how they make decisions about the targets of their research. Additional sub-sections below address the benefits of pharmaceutical investment in multiple drugs per class and the issue of public vs. private investment in pharmaceutical research.

A. Cost of Innovation

According to data from the National Science Foundation, pharmaceutical product development comprises one of the most research intensive sectors in the United States.⁹ The industry is one of the largest employers of scientists in the United States and its success or failure relies heavily on their ability to make breakthroughs.

Today, the process of bringing a drug to market takes 10 - 15 years on average. As a result, the average cost to develop a new drug has grown from \$138 million in 1975 to over \$800 million.¹⁰ The risks involved in the new drug development and approval

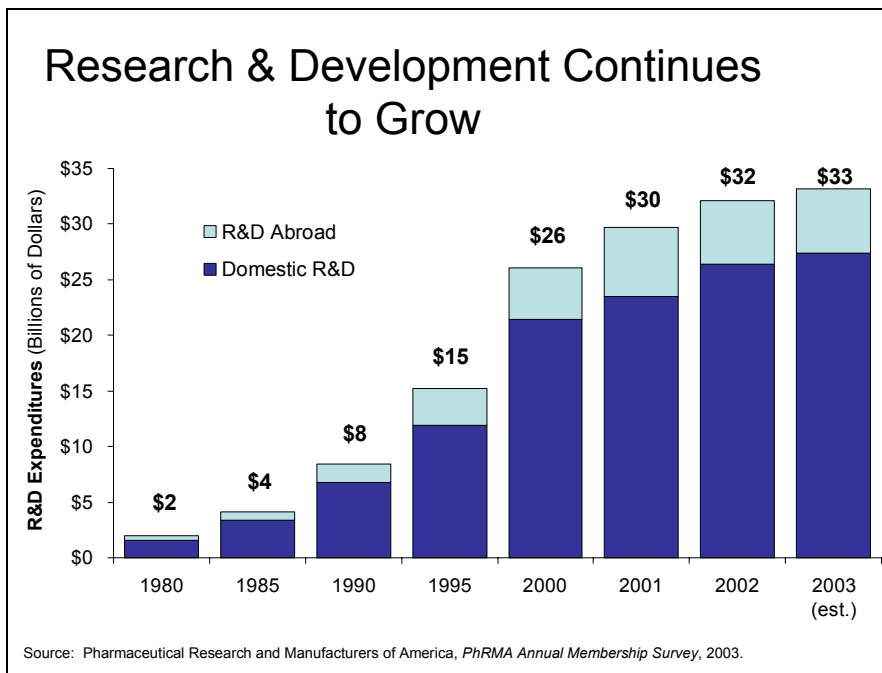
⁹ National Science Foundation, Research and Development in Industry, 1998. As quoted by: PriceWaterhouseCoopers, *The Critical Roles of R&D in the Development of New Drugs* (Washington, DC: PWC, 2001).

¹⁰ J. A. DiMasi, R. W. Hansen, and H. G. Grabowski, "The Price of Innovation: New Estimates of Drug Development Costs," *Journal of Health Economics* 22 (2003): 151–185.

processes are also substantial. Of every 5,000 molecules tested, only 250 drugs will enter preclinical testing, and only 1 is approved by the FDA. Only 3 out of 10 marketed drugs produce revenues that match or exceed average R&D costs. Yet a growing number of countries around the world nevertheless establish prices for innovative new drugs at exactly the same level as the price of older off-patent medicines. This is detrimental to funding research for new innovations.

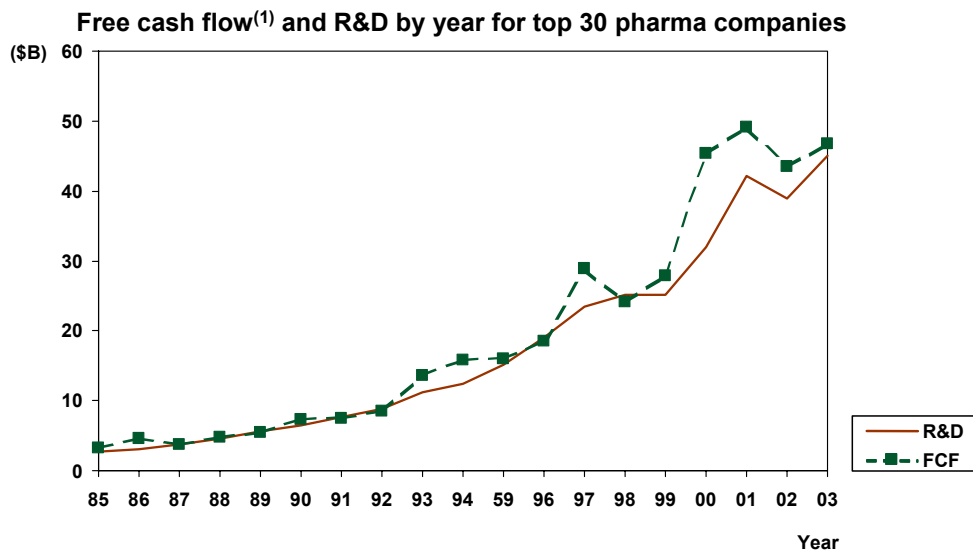
B. Level of Investment in R&D

Despite these risks and costs, over the past decade the value of the pharmaceutical industry's investment in research and development on new medicines has increased enormously.



Moreover, not only has the value of pharmaceutical research and development grown over time in absolute terms, it has also remained remarkably consistent in relative terms. Since 1985, the pharmaceutical industry has reinvested a relatively stable proportion of its free cash flow into research and development. A recent analysis by the Boston Consulting Group on this point produced the following figures (see Annex D for additional detail):

HISTORICALLY, INDUSTRY HAS MAINTAINED CLOSE RELATIONSHIP BETWEEN FREE CASH FLOW AND R&D SPEND



(1) EBITDA – Taxes – CapEx – Change in Working Capital
Source: Compustat; BCG Value Science center analysis of top 30 pharma companies

Last, it is important to note that four-fifths of pharmaceutical research dollars go toward “research for the advancement of scientific knowledge and development of new products and related services,” while only one-fifth goes toward “research oriented to significant improvements and/or modification of existing products.”¹¹ In fact, over the past five years new classes of drugs have been approved to treat AIDS, hypertension and angina, congestive heart failure, deep-vein thrombosis, blood clots, Type II diabetes, sepsis, bacterial infections, CMV, schizophrenia, and others.

C. Fruits of Innovation in the Pharmaceutical Industry

Over the past decade, pharmaceutical companies have pushed the scientific envelope, working at the cellular and molecular levels to dramatically advance the treatment of disease. At the end of 2002, 28 percent more medicines were being investigated by pharmaceutical companies for approval by the Food and Drug

¹¹ Pharmaceutical Research and Manufacturers of America (PhRMA), PhRMA Annual Membership Survey 2002 as cited in *Pharmaceutical Industry Profile* (Washington, DC: PhRMA, 2002).

Administration (FDA) than was true one decade before.¹² More than 1,000 medicines are now in the development pipeline.¹³

Between 1993 and 2003, more than 300 new drugs, biologics, and vaccines that prevent and treat over 150 conditions were approved by the FDA.¹⁴ The FDA also gave the go-ahead for numerous new indications for previously approved medicines, allowing physicians to tailor treatment strategies to meet a patient's individual disease status, past medication history, side effect tolerance, and preferences.

The new medicines that are the product of this decade of innovation have dramatically changed the "standard of care" for several major conditions. Medical treatment guidelines have been revised to recommend early intervention with these new, more effective medicines.

Throughout the decade, pharmaceutical companies shifted research to more complex diseases, clinical trial failure rates remained high, and a rigorous regulatory environment prevailed. The result of these growing demands on drug development has been an escalation in the cost to develop new drugs. Additionally, the marketplace has become more demanding, more patients qualify for treatment, and medicines are playing an increasing role in patient health care. All of these factors have contributed to the recent increase in prescription drug costs, even though prescription drug expenditures still make up only a small fraction of every dollar spent on health care.¹⁵ Years ago, diagnosis of rheumatoid arthritis (RA), HIV/AIDS, Parkinson's disease, Alzheimer's disease, schizophrenia, diabetes, high blood pressure, or high blood cholesterol often meant death following a terrible illness. Today, the picture is quite different. Many people with these conditions are able to lead productive, healthy lives, due in large part to the rapid pace of discovery and innovation in pharmaceutical treatments.

D. Benefits of Multiple Drugs in a Therapeutic Class

Notwithstanding these major advances, some have criticized the level of innovation in the pharmaceutical industry. As evidence, these critics point to the existence of multiple drugs in certain therapeutic classes and deride so-called "me-too" products. Foreign government pricing bureaucrats also too often mistakenly dismiss the value of such research. These critics do not understand the reality of the R&D process or the tremendous value to patients of having multiple drugs per therapeutic class.

To start with perhaps the most obvious point, companies rarely plan to be second to market with a new drug. Often research into certain diseases is proceeding

¹² Food and Drug Administration, "Number of Active INDs at the Close of the Calendar Year," 19 March 2003 <<http://www.fda.gov/cder/rdmt/cyactind.htm>> (5 August 2003).

¹³ Pharmaceutical Research and Manufacturers of America, *New Drugs in Development series* (Washington, DC: PhRMA, 2001–2003), available at <www.phrma.org/newmedicines>.

¹⁴ Pharmaceutical Research and Manufacturers of America, *New Drug Approvals series* (Washington, DC: PhRMA, 1994–2003) available at <www.phrma.org/newmedicines>.

¹⁵ Centers for Medicare and Medicaid Services, "The Nation's Health Dollar: 2001," 8 January 2003 <<http://cms.hhs.gov/statistics/nhe/historical/chart.asp>> (21 January 2003).

simultaneously in multiple companies in vigorous competition with one another. One company will no doubt get its product through the FDA hurdles and onto the market first. It would hardly make sense, or be in anyone's interest, for the second company to throw away the results of all its years of research, simply because by the time it got to market, another competing product was already there. Thus, the existence of multiple drugs per therapeutic class should never be automatically equated with a lack of innovativeness in the pharmaceutical industry – rather it is the result of vigorous marketplace competition that benefits patients in important ways. According to Janet Woodcock, MD, Director of the FDA Center for Drug Evaluation and Research (CDER), “The FDA would like to offer patients a choice of drugs within the same class, since not every patient responds to every drug in the same manner.”¹⁶

According to experts at Temple University School of Pharmacy, “Incremental advances, rather than ‘breakthrough’ discoveries, constitute the basic mechanism of all technological innovation. Newer drugs in a therapeutic class often have fewer side effects, improved drug safety and effectiveness, and greater ease of use which facilitates compliance with prescribed therapeutic regimens. Product alternatives permit treatments to be better tailored to individual patient needs.”

In addition, new uses for existing agents are continually discovered and bring significant benefits to patients. These improvements and discoveries are especially important for optimal treatment of elderly patients, because their diverse response to medications requires individualized care. A broad range of medicines provides physicians with a “tool chest” to treat each patient with precision and provide options when particular agents are ineffective or poorly tolerated by a given patient. Moreover, new, incremental innovations are often less expensive than existing agents in a therapeutic category, and some have been shown to save overall healthcare costs.¹⁷

For example, for diseases of the central nervous system, overall response rates are often 50% or less.¹⁸ Patients who fail to respond to one drug will often respond to another drug in the class. Examples of widely used drug classes associated with great variation in patient response are the selective serotonin reuptake inhibitors (SSRIs) and the non-steroidal anti-inflammatory agents (NSAIDs). In patients treated with SSRI agents for depression, 26% of non-responders to fluoxetine did respond to sertraline.¹⁹

¹⁶ T. Koppal, PhD, “How CDER's Janet Woodcock Helps Drug Companies Achieve Compliance, Speed the Drug Review Process, and Improve Time to Market for New Drugs,” *Inside the FDA*, 1 November 2002.

¹⁷ A. Werthemier, R. Levy, and T. W. O'Connor, “The Value of Incremental Pharmaceutical Innovation for Older Americans,” (Reston, VA: The National Pharmaceutical Council, December 2001).

¹⁸ U.S. Department of Health and Human Services, Agency for Health Care Policy and Research, *Treatment of Depression: Newer Pharmacotherapies* (Rockville, MD: AHRQ, 1999).

¹⁹ C.A. Zarate et al., “Does Intolerance or Lack of Response With Fluoxetine Predict the Same Will Happen With Sertraline?” *Journal of Clinical Psychiatry* 57 (1996): 67-71.

Conversely, another study reported that 63% of patients who failed to respond to sertraline did respond to fluoxetine.²⁰

The NSAIDs also differ greatly with respect to efficacy and patient tolerance. Often, multiple drugs must be tried before success is achieved. For example, in one two-year study of patients on NSAIDs, 49% of patients were switched to another NSAID; 20% were switched two times or more; and 7% received four or more different NSAIDs.²¹

The currently available beta-blockers offer differences in potency, cardioselectivity, effects on the nervous system, pharmacokinetic properties (which determine appropriateness for patients with impaired kidney or liver function), additional pharmacological benefits, potential for interaction with other drugs, efficacy in specific racial groups, complexity of the dosage regimen and adverse effects profile. The array of differences among these drugs allows for customized treatment for patients. This array of differences enables doctors to customize treatment to the patient's specific needs.²²

As these examples demonstrate, government policies that discourage multiple drugs per therapeutic class and simply steer all patients to the cheapest drug in a class overlook important patient consequences in favor of pure budgetary factors.

Finally, and as will be discussed more thoroughly in Section V.B, below, the existence of multiple drugs in a therapeutic class also exerts important cost-containment pressures through the competition mechanism of the private market. A study by Dr. Joseph A. DiMasi of Tufts University found that new drugs in a class are often priced lower than existing drugs in the class.²³ DiMasi examined the pricing of new entrants to drug classes and subclasses in eight therapeutic categories accounting for half of total retail prescription drug expenditures in 1999. The study found that the majority of new drug entrants he examined were launched at discounts (sometimes substantial) relative to both the class price leader and to the average price in the class. Of the 20 drugs examined, 13 were priced at discounts of at least 5%--and often at much larger discounts; five were introduced essentially at parity with existing prices; and two entered the market at a premium to the weighted mean price in the class but at a discount relative to the price leader in the class.

²⁰ M.E. Thase et al., "Fluoxetine Treatment of Patients with Major Depressive Disorder Who Failed Initial Treatment with Sertraline," *Journal of Clinical Psychiatry* 58 (1997): 16-21.

²¹ J. Jacobs and B.S. Bloom, "Compliance and Cost in NSAID Therapy," *Hospital Therapy*, suppl. (1987): 32-39.

²² A. Wertheimer, R. Levy, and T.W. O'Connor, "Too Many Drugs? The Clinical and Economic value of Incremental Innovations," National Pharmaceutical Council (NPC) (Reston, VA: NPC, 2001). (Reprinted from *Research in Human Capital and Development: Investing in Health: The Social and Economic Benefits of Health Care Innovation*, 14 (2001): 77-118).

²³ J.A. DiMasi, "Price Trends for Prescription Pharmaceuticals: 1995-1999," Background report prepared for the U.S. Department of Health and Human Services' Conference on Pharmaceutical Pricing Practices, Utilization and Costs (Washington, D.C.: August 8-9, 2000).

Brand-to-brand competition is vigorous and coming earlier in the life cycle of breakthrough drugs and competition between branded drugs is at least as vigorous as between brands and generics. For example, Tagamet®, an ulcer drug introduced in 1977, had six years on the U.S. market before the first competitor in the same class, Zantac®, was introduced. In contrast, Invirase®, the first in a new class of HIV antiretroviral drugs known as protease inhibitors, was on the market only three months before a second protease inhibitor, Norvir®, was approved.

Managed care organizations have stated the value of multiple drugs in a therapeutic class to help drive down costs. In a May 24, 2002, letter to the National Association of Insurance Commissioners, the Blue Cross Blue Shield Association and other managed care organizations cited competition “among therapeutically similar drugs” as “creating the potential for driving down the cost of the class of drugs.” While we do not endorse the letter’s proposals, and it is also important to recognize the differences among patients in its responses to medicines, its observations regarding the economic value of multiple drugs in a class are important to note.

Thus, for cost as well as patient care reasons, foreign government policies that depress innovation – including R&D directed toward producing additional drugs in existing therapeutic classes -- should be a major cause for concern for policymakers.

E. Role of Public vs. Private R&D in the Pharmaceutical Sector

Innovation in the research-based private sector pharmaceutical industry is by far the primary source for discovery of new drugs around the world. In the United States, the National Institutes of Health (NIH) conducts important basic research on biomedical questions and technologies, but that research -- by itself -- rarely results in innovative new medicines that benefit U.S. patients.

According to a 2001 NIH report²⁴, although NIH’s federally funded research has contributed in a substantial way to advances in medicine and biology, its direct contributions to a final therapeutic product is “limited and difficult to determine” due to many factors: (1) Technologies developed in basic research labs often require further development; (2) Not all technologies arising from NIH funded research lead to therapeutic drugs. (As NIH notes, “new chemical entities that lead to therapeutic products are hard to discover...”); (3) The likelihood that a compound will reach market is very low;²⁵ and (4) Development and production of a FDA-approved therapeutic drug occurs, on average, eight to twelve years after a license is signed, and a license offers no guarantee that a product will ever reach the market.

24 National Institutes of Health, *A Plan to Ensure Taxpayers’ Interests are Protected*, NIH Response to the Conference Report Request for a Plan to Ensure Taxpayers’ Interests are Protected (Washington, D.C.: NIH, July 2001).

25 Ernst and Young, *Convergence: Ernst and Young’s Biotechnology Industry Report, Millennium Edition*, (30 October 2000).

As noted by former NIH Director Varmus, “[T]here is an important distinction between having rights to a compound and having rights to a fully developed product. NIH does not license drugs that are ready for marketing. NIH biomedical technologies are early stage and, in almost all cases, require further research, development, and testing, usually in combination with other proprietary technologies, to bring a product to market.”²⁶

Over the past few years a number of studies have examined NIH’s role in developing new drugs. According to a study conducted by NIH at the direction of Congress, only four of 47 drugs having \$500 million in sales in the United States were developed in part with NIH funding. And none of these top-selling drugs was developed solely with public funds.²⁷

The story does not change when one looks at all new drugs, not just top sellers: the pharmaceutical industry is responsible for over 90 percent of new drugs. A 1993 study published in the *Journal of Clinical Pharmacology* found that during 1981-1990, the pharmaceutical industry was the source for 181 of the 196 new drugs approved by the Food and Drug Administration (FDA) (92.4 percent), academia was the source of seven percent of the drugs (3.6 percent), and the government was the source of two of the drugs (1 percent).²⁸

The importance of private sector pharmaceutical research is even more apparent when one looks at the figures for the 1990s. Between 1991 and 2001, 339 new drugs were approved by the FDA. According to an NIH report issued by the Office of Technology Transfer, from 1991 to October 1, 2001, 15 FDA approved therapeutic drugs and vaccines were developed with technologies from the intramural research program at the NIH.²⁹ In other words, only four percent of all approved drugs between 1991 and 2001 were developed with technologies from the intramural program at the NIH.

These figures do not mean, however, that NIH research is unproductive. Rather, the key is that the focus of that research is simply different than privately-funded commercial research undertaken by the innovative U.S. pharmaceutical industry. Moreover, a study done in May 2000 by the U.S. Congressional Joint Economic Committee (JEC) entitled, *The Benefits of Medical Research and the Role of NIH*, examined the role of federal funding for medical research and the benefits that derive from that research. The Committee report states that although the rate of return on

²⁶ Letter from Dr. Harold Varmus, Director National Institutes of Health, to Consumer Project on Technology (19 October 1999).

²⁷ *A Plan to Ensure Taxpayers’ Interests are Protected*, op cit.

²⁸ K. Kaitin, N. Bryant, and L. Lasagna, “The Role of the Research-Based Pharmaceutical Industry in Medical Progress in the United States,” *The Journal of Clinical Pharmacology* 33 (1993): 412-417.

²⁹ U.S. Food and Drug Administration, “FDA Approved Therapeutic Drugs and Vaccines Developed With Technologies From the Intramural Research Program at The National Institutes of Health as of October 1, 2001,” 1 October 2001, <http://ott.od.nih.gov/NewPages/therapeutics.pdf> (accessed March 27, 2002).

publicly funded research is difficult to quantify, the benefit of increased life expectancy in the United States as a result of advances in health care creates annual net gains of about \$2.4 trillion (using 1992 dollars). The Committee concluded, “if only 10 percent of those increases in value (\$240 billion) are the result of NIH-funded medical research, it indicates a payoff of about 15 times the taxpayers’ annual NIH investment of \$16 billion.”³⁰ The JEC report also cites estimates that have been made in econometric studies that place the economy-wide rate of return on publicly funded research at 25 to 40 percent a year. The NIH report noted, “The conclusion of these and other studies on the issue of return on investment are consistent and comparable in that they assert that there are both monetary and intangible benefits of remarkable value that are gained from federally funded research.”³¹

As noted, the NIH’s role in supporting U.S. innovativeness is extremely important, but distinct from the process of drug development. It is notable that Europeans have evidenced no comparable commitment to supporting the basic biomedical sciences through their public institutions. An important study commissioned by the European Commission in 2000 demonstrated that Americans are conducting significantly more pharmaceutical-related research in universities and public institutions as compared to their European counterparts.³² “Europe has been weaker because we have not invested enough,” said Luciano Maiani, Director, European Organization for Nuclear Research (CERN). Only Finland and Sweden have reached the E.U. goal of spending 3% GDP on research. If the whole E.U. were to hit that target by 2010, R&D investment must grow by 8% a year – nearly twice the 4.5% annual increase recorded since 1997. This doesn’t appear to be happening though. For example, in Italy, public-research spending has fallen over the past decade.³³

Even in European institutions that have spent more on R&D, the levels still pale in comparison to the United States. According to Colin Blakemore, head of Britain’s Medical Research Council (MRC), “there’s simply no comparison to the U.S.” The \$27 billion annual budget of its U.S. counterpart the NIH, is about 40 times that of the MRC. Even corrected for population, it is 12 times higher. The total annual MRC budget in 2003 was equal to one-fifth of the increase in the NIH budget, according to Blakemore.³⁴

F. Costs of R&D vs. Promotional Expenses

In considering the effect of foreign price controls on innovation, and the pharmaceutical industry’s commitment to innovation, U.S. Government agencies should be aware of the existence of numerous false claims regarding the relative magnitude of

³⁰ The Joint Economic Committee, U.S. Senate, *The Benefits of Medical Research and the Role of the NIH*, May 2000, <http://jec.senate.gov>.

³¹ NIH Contributions to Pharmaceutical Development. Administrative document prepared by NIH Staff, February 2000.

³² A. Gambardella, L. Orsenigo, and F. Pammolli, *Global Competitiveness in Pharmaceuticals: A European Perspective*, report prepared for the Directorate General Enterprise of the European Commission (Brussels, Belgium: Enterprise of the European Commission, November 2000).

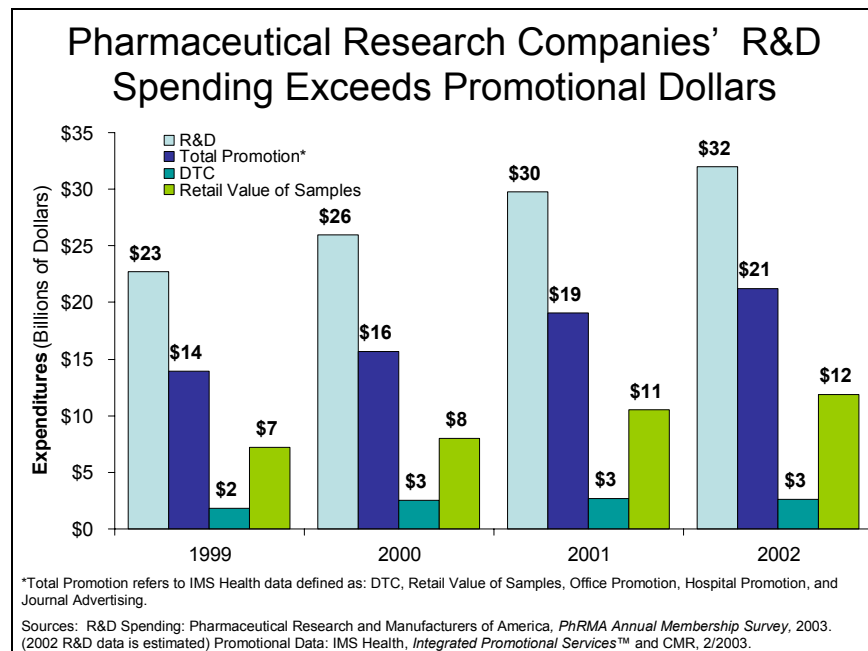
³³ Ibid.

³⁴ Ibid.

the industry's investment in R&D and the industry's spending on promotional expenses. Contrary to the ill-founded criticisms of some interested parties often repeated in the press, the U.S. pharmaceutical industry spends substantially more on research and development than on advertising and other promotional expenses.

A report issued by the General Accounting Office (GAO) on direct-to-consumer (DTC) advertising confirmed that pharmaceutical companies spend more on R&D than on DTC advertising and other types of promotion.³⁵ According to the data cited by GAO, in 2001 companies spent \$30.3 billion on R&D and \$19.1 billion on all promotional activities, including \$2.7 billion on DTC advertising.³⁶ In 2002, industry R&D rose to \$32 billion, and DTC advertising amounted to approximately \$3 billion. Total promotion amounted to \$21 billion in 2002. More than half of total marketing expenses went to providing free samples to doctors, who often distribute them to their low-income patients in particular. In total, less than two percent of total U.S. sales went for DTC advertising.

The chart below illustrates the relative value of industry spending on R&D and promotional activities. It demonstrates that over the past several years, research-based pharmaceutical manufacturers generally spent over ten times as much on R&D as they did on DTC advertising.



³⁵ U.S. General Accounting Office, *Prescription Drugs, FDA Oversight of Direct-to-Consumer Advertising Has Limitations*, (Washington, D.C.: GAO, October 2002): GAO-03-177; According to the report, GAO relied on industry analysis in reaching this conclusion, but it also stated that “researchers have consistently cited these data sources and they represent the best available information.”

³⁶ See also NDC Health, “Pharma Trends 2001 Year in Review,” 8 March 2002 (reporting similar data demonstrating that the pharmaceutical industry spent \$2.8 billion on direct-to-consumer (DTC) advertising in 2001).

Nor should the absolute level of promotional spending of the industry be cause for concern. Research indicates that DTC advertising helps educate patients about medical conditions and treatment options, encourages dialogue between patients and physicians, and promotes improved compliance with physician-prescribed treatments. It provides consumers with the information needed to ask their doctors questions about symptoms or new medicines that might help them. DTC advertising also reminds people to take medicines and get their prescriptions refilled when needed.

Last, according to numerous reports and studies, there is no direct relationship between DTC advertising and the price growth of drugs. A recent Federal Trade Commission (FTC) report confirms this view, and found that “DTC advertising accounts for a relatively small proportion of the total cost of drugs, which reinforces the view that such advertising would have a limited, if any, effect on price.” The report continues by stating, “The informative nature of DTC advertising, as revealed by the consumer and physician surveys, also tends to undercut the argument that expenditures on DTC advertising are passed on to consumers in the form of higher drug prices... Consumers receive these benefits from DTC advertising with little, if any, evidence that such advertising increases prescription drug prices.”³⁷

Nor does DTC advertising drive inappropriate utilization of pharmaceutical products. For example, a 2002 study on cholesterol-lowering statins, which are DTC-advertised found that there is “no statistically significant effect from any form of advertising and promotion on any new statin prescription or renewals and no evidence of adverse marketing effects from advertising...”³⁸ These findings are supported by another recent study that looked at whether pharmaceutical marketing has led to an increase in use of medications by patients with marginal indications. The study found that high-risk individuals were receiving lipid-lowering treatment “consistent with evidence-based practice guidelines” despite the fact that “a substantial portion of patients continue to remain untreated or undertreated...”³⁹

G. Conclusion

In this section, we have attempted to provide government policy makers with relevant background data regarding the level of research and innovation in the U.S. pharmaceutical industry today. PhRMA members have demonstrated a remarkable commitment to the process of innovation for decades, notwithstanding the high costs and enormous risks associated with pharmaceutical research and development. It is precisely

³⁷ Federal Trade Commission, Comments of the Staff of the Bureau of Consumer Protection, the Bureau of Economics, and the Office of Policy Planning of the Federal Trade Commission, Before the Food and Drug Administration: In the Matter of Request for Comments on Consumer-Directed Promotion (Docket No. 2003N-0344) (V040002) (December 2003).

³⁸ J. Calfee, et al., “Direct-to-Consumer Advertising and the Demands for Cholesterol-Reducing Drugs,” *The Journal of Law and Economics* (October 2002).

³⁹ R. DuBois, et al., “Growth in Use of Lipid-lowering Therapies: Are We Targeting the Right Patients?” *The American Journal of Managed Care* 8 (October 2002): 10, 862-867.

this commitment that European and other foreign governments have taken for granted. Their restrictive policies consistently discriminate against innovative products and have served to depress the level of innovation in the industry over the past decade. The broader effects of these restrictive policies are the subject of the following section.

V. Effects of Foreign Price Controls and Other Market Access Barriers

Many of the foreign price controls and access barriers described in Section II of this Submission systematically discriminate against innovative pharmaceutical products. Generally the discrimination operates by delaying the introduction of new, innovative medicines, and systematically limiting the prices and volumes for new innovative medicines below levels that would be set by a competitive marketplace. These systems almost completely ignore the massive investment of R&D necessary to invent and develop a new medicine, and have profound consequences for patients, both in those foreign countries and in the United States. These practices have also had and continue to have serious effects on the global pharmaceutical industry, on the economies of those countries that impose the short-sighted measures, and on the national economy of the United States. The following section details these ultimate effects on patients and other segments of the U.S. economy.

This section references several sources in support of its conclusions. Two of those sources are attached as Annex C and D to this submission. Annex C is a literature review conducted by Professor Daniel Kessler of Stanford University, the Hoover Institution and the National Bureau of Economic Research. Professor Kessler recently published this essay after conducting an extensive review of the empirical studies in the economic literature addressing the effects of pharmaceutical price regulation. Professor Kessler's conclusion is telling: "empirical research finds that price regulation has adverse effects on the cost and quality of care."

Annex D contains a White Paper released July 1, 2004 entitled, "Adverse Consequences of OECD Government Interventions in Pharmaceutical Markets on the U.S. Economy and Consumer," from a BCG analysis commissioned by PhRMA. The materials in Annex D summarize the results of the BCG analyses of several discrete issues concerning the effects of pharmaceutical price controls on U.S. markets and consumers.

PhRMA hopes that all of this analytical information is useful to the Administration in drafting its report to Congress on the effects of foreign price and access controls. As described in more detail below, we firmly believe that such price control measures represent free-riding by foreign governments on U.S.-led R&D investment, and have caused measurable harm to U.S. consumers and the U.S. economy in terms of reduced access to and development of innovative medicines.

A. Effect of Foreign Price and Access Controls on Trade: Discrimination Against Innovation, Barriers to Market Access and Diminished Intellectual Property Protection

Section II of this Submission, as well as Annexes A and B, described in factual terms the price and access controls imposed by OECD governments to restrict the pharmaceutical market in those countries. This section describes how these policies constitute non-tariff barriers to international trade. In sum, these policies often discriminate against innovative products (which also tend to be heavily imported products), restrict market access to U.S. pharmaceuticals, and undermine the value of patent protection in those markets.

1. Discrimination Against Innovation

Foreign government price and access controls often discriminate against innovative products and favor local producers of non-innovative pharmaceuticals and other local players in the health care system. Countries without a local pharmaceutical industry tend to rely particularly heavily on price controls on innovative pharmaceuticals to balance their health care budgets. Local interests -- such as generic producers, wholesalers and pharmacists -- generally occupy a favored position within these systems. For example, reimbursed prices for generic pharmaceuticals -- often produced primarily by domestic companies -- are often quite high (70 percent -- 90 percent of the value of the innovative product is not unusual). These figures represent a significant distortion of a market-based result, in which the average price of generics is much lower. While such discrimination may or may not be between "like products" within the meaning of GATT national treatment obligations, it is nevertheless unfair and prejudicial to American interests.

Examples: Italy passed a law in 2002 imposing a blanket five percent price decrease for all pharmaceuticals priced above a certain threshold. The impact of the price decrease fell overwhelmingly on the research-based pharmaceutical industry that produces higher-value medicines and is, not coincidentally, largely foreign based. More recently, in 2003, Italy passed a new rebate scheme pursuant to which pharmaceutical manufacturers are responsible for repaying to the government any amount by which public spending on pharmaceuticals exceeds government budget targets for such spending. For clear political and protectionist reasons, local pharmacists and distributors (whose fees are included within the budgetary spending targets) have nevertheless been exempted from the payback obligation.

In *Canada*, the Patented Medicines Price Review Board, as its name suggests, monitors the prices of only patented medicines, which are far more likely to be imported than generic products. Generic producers are exempt, and not coincidentally, the domestic Canadian pharmaceutical industry is largely a generic one.

In *Australia*, the prices paid by the government's Pharmaceutical Benefits Scheme to local pharmacists are indexed for inflation, and rise every year. The Australian government has adamantly opposed allowing any such adjustment for inflation for pharmaceutical products which, again, are largely developed abroad and imported into the country.

2. Delay and Denial of Effective Market Access

Foreign price control mechanisms also operate to deny market access to U.S.-made products. They do so in two ways: (1) by delaying the availability of new products; and (2) by denying the availability of new products.

Given that foreign national health insurance schemes typically dominate the domestic market for pharmaceuticals, a product effectively cannot be marketed in a country until the national authorities have determined its reimbursement price. The price control bureaucracy in almost every country is a highly opaque one and the process of obtaining a government-approved price can be lengthy. These processes operate to delay market access (and diminish the effective patent term) for many U.S. medicines. Governments often delay adding new products to national reimbursement lists merely to avoid the cost of providing those treatment options to patients.

Examples: The government price control bureaucracy in several western European countries routinely delays market entry for new products by over one year.⁴⁰ In Austria, Finland, France, Greece and Portugal, for example, it takes on average between 332 and 404 days to get an *approved* new drug on the government reimbursement lists.⁴¹

A report by the G10 Medicines Group, which reviewed the impact of governmental pharmaceutical, health and enterprise policies in Europe, recommended reducing the time between granting a marketing authorization and pricing and reimbursement decisions. According to the report, "The price negotiating systems and reimbursement structures in a number of Member states can lead to significant delays."⁴²

Similarly, a study that examined regulatory delays in Canada, entitled *Prescription Drug Costs: Has Canada Found the Answer?*, found that one way Canada tries to control costs is by dragging out the process of approving expensive new drugs, no matter how beneficial they are.⁴³ The federal approval process takes 13 percent longer than in the United States. The study also found that, "Even if a drug wins federal approval [in Canada], it faces 10 more hurdles - the 10 provinces. Each province has a

⁴⁰ Cambridge Pharma Consultancy, *Delays in Market Access* (December 2002).

⁴¹ Cambridge Pharma Consultancy, op. cit. The study examined 78 medicinal products for which marketing authorization was granted between January 1, 1997 and June 30, 2001.

⁴² European Commission, "High Level Group on Innovation and Provision of Medicines, Recommendations for Action," G 10 Medicines Report (Brussels, Belgium: European Commission, 7 May 2002).

⁴³ W. McArthur, "Prescription Drug Costs: Has Canada Found the Answer?" National Center for Policy Analysis (Washington, D.C.: National Center for Policy Analysis, 19 May 2000): Brief Analysis No. 323.

review committee that must approve the drug for its formulary. Of 99 new drugs approved by the federal government in 1998 and 1999, only 25 were listed on the Ontario formulary. Further, the provincial approval times vary greatly from province to province. The wait for approval in Ontario is nearly 500 days.” The chart below illustrates the scope of the problem.

Average Time to Listing for Full and Restricted Listings
Comparison of 2-year and 5-year data

	2 year data		5 year data	
	N*	Average TTL** (Days)	N*	Average TTL (Days)
BC	17	472	86	465
ALTA	27	432	102	421
SASK	31	371	127	404
MB	30	541	129	506
ON	18	506	85	524
QC	37	415	143	349
NB	13	619	71	595
NS	24	455	111	581
PEI	14	776	55	973
NFLD	6	592	59	637
NIHB	19	362	86	479

*N = Number of submissions approved
**TTL= Time to Listing

Source: IMS Health 2003.

Furthermore, recent policy changes in Canada appear likely to make the situation worse. As of 2003, the provinces and the federal government have set up a Common Drug Review (CDR) process intended to improve efficiency and reduce timelines. Based on a cost-effectiveness analysis, the CDR can only make listing recommendations and the provinces still require additional budget impact assessment to make their own decision about the type of listing they will grant. Though the system has only recently been implemented, the CDR seems to add one more hurdle and therefore lengthen time to access to market rather than shorten it. Most provinces already have a variety of restrictive levels of listing if and when they decide to list the product at all.

Sometimes these delays become so lengthy as to turn into effective denials of market access. It is unfortunately not uncommon for some foreign governments to make a policy decision to close reimbursement lists altogether to innovative pharmaceuticals. Poland and China are the most recent examples of such actions, as neither country has added any new products to government reimbursements lists since 1998.

In addition, as discussed in Section II of this Submission, many governments use highly restrictive formularies to control their citizens’ access to new medicines. Such an approach is bad policy and bad medicine. A patient’s reaction to a medicine can be highly individual and the effects of a drug can vary across populations. Nevertheless, some governments are willing to substitute their judgments for doctors’ judgments, and

impose a one-size-fits-all approach with respect to certain medical needs by approving only one (or very few) pharmaceutical products to treat particular conditions. From a practical perspective, makers of competing products are effectively shut out of the market. Another way in which governments restrict market access is by imposing stringent *reimbursement guideline restrictions* (i.e., reimbursement only allowed for a range of uses much narrower than that the drug for which the drug has been medically approved). This practice is widely followed in Korea and Australia.

Example: New Zealand has long had one of the most restrictive formulary systems in the world. The government directly controls 75% of the market in New Zealand, and indirectly controls the rest. It typically permits very few medicines per therapeutic class. Market access for many competing products that treat the same condition is effectively and completely denied. In general, New Zealand denies reimbursement listing if its authorities believe sufficient alternative products exist, denies or conditions initial listing on the manufacturer's agreement to set the introductory market price at the reimbursement level, denies or conditions listing on the manufacturer's acceptance of a reimbursement level that is less than or equal to existing medicines, and conditions an initial reimbursement level of a new medicine to the price of an older one. Over the past three years, New Zealand has approved an average of just *four* new drugs per year for reimbursement, whereas about 30 new drugs per year were launched in other developed country markets.⁴⁴ In short, nearly 90 percent of new drugs launched in the past three years have been effectively kept off the market in New Zealand. As a result, several pharmaceutical companies have announced publicly that they have almost completely abandoned the New Zealand market over the past five years.

3. Undermine Intellectual Property Rights

Finally, these government intervention strategies in the pharmaceutical marketplace drastically undermine the value of intellectual property protection in those markets.

A patent right that gives the patent holder the exclusive right to sell his invention in a market, but that is limited by a requirement that the product be sold at marginal cost, is of little commercial value to the right holder. A country cannot be said to adequately and effectively protect intellectual property within the meaning of the trade statutes if that country puts in place regulations that effectively nullify the value of the patent rights granted.

The United States routinely treats weak foreign intellectual property laws as a major trade issue. Indeed, the entire rationale for the WTO TRIPS Agreement was that international free-riding on innovation is a kind of trade barrier. Allowing copycat manufacturers to pirate U.S. intellectual property, whether it is embodied in software, audiovisual recordings or medicines, undermines the export possibilities of those industries. Foreign laws that allow free-riding through other means – i.e., price and

⁴⁴ Researched Medicines Industry Association of New Zealand, 2004.

volume controls – equally diminish the value of U.S. intellectual property rights and hurt U.S. exporters that rely on intellectual property protection.

As described earlier, many countries around the world practice “reference pricing”. This means that the price of a new drug is tied, by law, to the price of other older and often off-patent medicines. These older medicines may have different benefits and side-effects than the new innovative products. *By design*, these systems are set up to compensate innovative products at the same rate as generic products, and undermine the value of pharmaceutical patents in that market.

The delays caused by the need to go through the bureaucratic pricing process, described above, also undermine the value of pharmaceutical patent holders’ intellectual property. By delaying market access, these regimes waste potentially valuable patent term that cannot be recovered by the patent holder.

Example: Under *Australia’s* system, government prices for new medicines are often set by reference to existing medicines in a therapeutic class, regardless of whether those other medicines are generic products or not. The link with these older drugs continues year-after-year, so that when a referenced drug goes off-patent and its price falls, the price of the newer drug that is still on patent is significantly diminished as well. The end result is that there is little reward for innovation.

Japan follows an analogous practice, with similarly anti-innovation results. Reimbursement prices for innovative new medicines are set by the government through the use of older, generic “comparator products,” the prices of which have been reduced over the years. As a result, the granted prices for new products are often even less than the prices of their comparators at the time the comparators were introduced.

For all of these reasons, PhRMA believes foreign government price and access controls constitute non-science-based, non-tariff barriers and surely undermine the export potential of this major U.S. industry. Advocacy against foreign government price and access controls on pharmaceuticals should be a core plank of the U.S. Government’s trade policy going forward. Beyond these traditional effects on trade, however, foreign price and access controls on pharmaceuticals have even more damaging effects on patients around the world and the U.S. health care sector and economy as a whole, as detailed in the following sub-sections of this Submission.

B. Effects on Patients: Delayed and Denied Access to Innovative Medicines and Higher Prices

Foreign price controls have significant negative ramifications for patients in the United States and in other developed countries.

1. U.S. Patients

One of the most serious negative effects of foreign price and access controls for U.S. patients is a reduction in the number of innovative new drugs that would be available in the absence of foreign price controls. Beyond the health consequences of foregoing these new medicines, there is another important consequence on prices. Economic analysis suggests the existence of a “competition effect,” pursuant to which the entry of additional drugs into a therapeutic category of medicines exerts downward pressure on prices. Both of these effects are addressed below.

a. Reduced Levels of R&D Produce Fewer New Drugs

The discriminatory practices of foreign governments against new innovative pharmaceuticals depress the incentives for future innovation that would occur in the absence of such government price controls. By reducing the level of pharmaceutical research, government price controls directly reduce the number of new medicines that are discovered. Patients in the United States (and around the world) are thereby denied treatments for conditions and diseases for which no adequate or effective therapy currently exists. Patients are also denied the benefits of medicines that, while similar to existing medicines, may have fewer side effects or other valuable benefits such as improved administration or easier dosing.

BCG examined the impact foreign price controls have on limiting pharmaceutical innovation here in the United States. The BCG analyses and conclusions reinforce this point of price controls hampering innovation (see Annex D). BCG established a straightforward set of assumptions to quantify this effect;

First, the analysis began with the assumption that in the absence of foreign price and access controls the global returns to innovative drugs would be higher. BCG found that without the administrative barriers and restrictive pricing imposed by OECD market interventions, the returns earned by successful innovative drugs would probably increase by 35-45 percent.⁴⁵

Second, incremental capital, attracted by the higher returns, would flow into R&D investment. In support of this assumption, BCG observed that the industry has a record of reinvesting a steady proportion of its free cash flow back into R&D (see Section IV.B. or Exhibit 19 in Annex D);⁴⁶ and that historically, where changes in regulations or the environment have modified incentives, the industry has responded quickly. A key example is the Orphan Drug Act, passed in 1983, where new rewards were created for a particular kind of R&D investment (diseases with <200K patients), and considerable investment resulted. Many new medicines were created as a result of this increased R&D.⁴⁷ Assuming a conservative annual base of \$38 billion invested globally in R&D

⁴⁵ See Exhibit 18 in Annex D, “Summary: OECD Price Controls Cost Biopharma Industry 35%-45% Incremental Revenues.”

⁴⁶ Source from BCG analysis, Compustat; BCG Value Science center analysis of top 30 pharma companies.

⁴⁷ FDA, Office of Orphan Drug Products, “Orphan Drug Act – Implementation and Impact.”

directed at research on NCEs, and assuming that R&D investment were to increase in proportion to the higher revenues, there would be an additional \$13 - 17 billion in R&D spend per year.⁴⁸

Third, as a consequence of the increased R&D spend, there would be many more drugs introduced into the market. The economic literature supports the proposition that changes in R&D expenditures affect the rate of discovery of new drugs. Based on data on 28 firms from 1969-79, Jensen (1987) shows that R&D expenditures have a significant, positive effect on the number of NCEs discovered.⁴⁹ Taking this logic the next step, BCG estimated that – given about \$13-17 billion in incremental R&D spend, and using BCG’s estimated average R&D cost per drug of \$1.3 billion in 2002– there would be an additional ten to thirteen new drugs launched per year.⁵⁰ (It is important to note that DiMasi found that the cost to develop a new medicine was \$0.8 billion in 1997. BCG inflated this figure forward assuming a real growth rate of 7 percent.) BCG concludes that, factoring in the industry’s historical R&D spend and productivity, there would be an estimated incremental stock of 110-140 additional branded drugs available today that would have been launched over the past decade had it not been for OECD country price controls. BCG concludes that, “Applying these averages to the incremental stock of innovative drugs, our analysis suggests further that, without OECD controls, there would be about 35-40 entirely new drug classes today. History demonstrates new therapeutic categories are opened, significant clinical and economic benefits have emerged.”⁵¹

The analysis by BCG demonstrates that as a result of foreign government price controls, U.S. consumers currently forgo new developments that would have been made had these price controls not been in place in OECD markets.

Other economists have reached complementary conclusions regarding the impact of price and access controls on pharmaceutical R&D and the number of new drugs discovered. According to Professor John Vernon of the University of Connecticut, price controls and other equivalent regulation will reduce expected return on investment in R&D, and therefore the demand for R&D. Vernon states "pharmaceutical price regulation in the United States would lead to a reduction of between 36.1 and 47.5 percent in industry R&D intensity."⁵² He concludes that, "new price regulation in the U.S. could impose a very high cost in terms of foregone medical innovation."⁵³ Vernon

⁴⁸ During 2002, there was approximately \$38 billion in R&D spending on NCEs (U.S., Europe, Japan). Multiplying the incremental revenues by the annual R&D spending figure yields \$13 to \$17 billion in incremental annual R&D spend on NCEs.

⁴⁹ E. Jensen, "Research Expenditures and the Discovery of New Drugs," *Journal of Industrial Economics* 36 (1987): 83-95.

⁵⁰ See Exhibit 22 in Annex D, "Impact of OECD Eliminating Cost Controls: Incremental Drug Output."

⁵¹ Annex D: BCG White Paper, "Adverse Consequences of OECD Government Interventions in Pharmaceutical Markets on the U.S. Economy and Consumer."

⁵² J. Vernon, "Drug Research and Price Controls," *Regulation* (Winter 2002-2003).

⁵³ *Ibid.*

has also estimated that if price controls had been in place between 1980 and 2001 in the United States, between 330 and 365 new medicines would not exist today.⁵⁴

b. Reduced R&D Also Likely to Affect U.S. Prices

Another direct and more tangible consequence of foreign government pharmaceutical price and access controls on pharmaceuticals is that, based on accepted economic theory, it appears that prices for U.S. consumers would likely be lower if price controls in OECD markets are lifted. The reason is the “competition effect” or the effect of market forces that drive down prices when there are multiple competitors in the same therapeutic class. As more medicines are developed and launched within the same class, the result is likely reduced prices of medicines in that class because of these competitive market forces.

It is not possible for PhRMA to provide to the Commerce Department directly observed data demonstrating this effect based on the behavior of our member companies. As government policy makers can appreciate, the actual prices and rebates agreed between pharmaceutical companies and their customers are highly confidential and that information is never collected or discussed at PhRMA, nor is it publicly available. The economic literature, however, contains a number of studies demonstrating the pricing effect described. Moreover, straightforward economic theory also predicts this result. Interestingly, both economic theory and the studies on this topic both point in the same general direction; that historically, prices fall when there are additional entrants within the same class.

If, as BCG finds, there would be an additional 10 to 13 new medicines made available each year as a result of lifting foreign government price controls, the result would be more medicines competing against one another in the marketplace. The U.S. market is comprised of large purchasers such as PBMs that insure millions of lives and have the ability to aggressively negotiate directly with pharmaceutical manufacturers. This has the effect of valuing products based on market forces. Published studies have examined the impact of these market forces on price when drugs are launched within the same class. An article published by Lu and Comanor suggests that increased competition within a drug class leads to lower list launch prices.⁵⁵

Other studies confirm the impact of large numbers of competitive entrants driving down prices.⁵⁶ An article by Lee published in the *New England Journal of Medicine* found that prices for medicines are often lower than the first medicine in a class. Lee finds that additional entrants in a market, “reflect and create competition among drug and device manufacturers, and that competition is also a powerful driver of better quality and

⁵⁴ C. Giaccottoo, R. Santerre, and J. Vernon, “Explaining Pharmaceutical R&D Growth Rates at the Industry Level: New Perspectives and Insights,” AEI-Brookings Joint Center for Regulatory Studies, (December 2003): Publication 03-31.

⁵⁵ Z.J. Lu and W.S. Comanor, “Strategic Pricing of New Pharmaceuticals,” *The Review of Economics and Statistics* 80 (1998): 1, 108-118.

⁵⁶ W. D. Reekie, “Medicine Prices and Innovations: An International Survey,” The Institute of Economic Affairs (London, England: 1996).

lower costs.”⁵⁷ Lee uses the statin therapeutic class as an example of what occurs to price as additional entrants are introduced within the same class. According to Lee, the first statin entered the market in 1991 at \$137.56, the second statin entered the market at \$109.31 in 1996, and the third entered the market in 2003 at \$75.60.⁵⁸ The above retrospective analyses are illustrative of the point that as there are additional entrants in a class, prices decline.

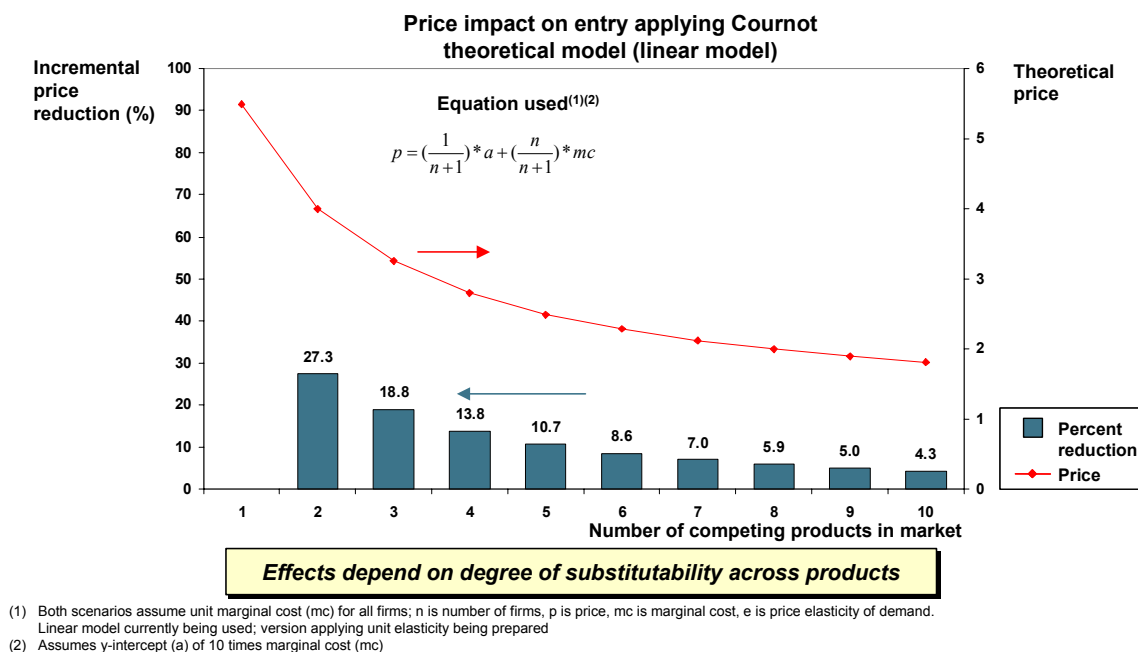
In addition to the published literature, economic theory also predicts that prices would decline with additional entrants in a market. The BCG analysis suggests the importance of examining the Cournot model and what it says about the effect on price of adding additional entrants into a market. The Cournot economic theory provides that as more companies enter with products in a market, prices will fall.

The Cournot model does require certain strong assumptions; however, it remains the best available mechanism for modeling likely firm behavior under these circumstances. Under Cournot, products are assumed to be completely substitutable, however, even within the narrowly defined classes, drugs are differentiated across efficacy and side effect profiles. Additionally, there is some cross substitution across classes. Under Cournot, the total market is assumed to be relatively stable, while in reality, for most classes with new entrants, drug consumption is typically growing. Notwithstanding these limitations, using the Cournot model is the best available solution to model a widely recognized phenomenon in the absence of directly observed data. These limitations do imply, however, that the model provides a theoretical upper bound on potential price impact. The following slide from the BCG study shows the theoretical implications of the Cournot model on pricing in a hypothetical market with additional entrants.

⁵⁷ L. Thomas. “Me-Too” Products—Friend or Foe?” *New England Journal of Medicine* (15 January 2004): 211-212.

⁵⁸ Ibid.

THEORETICAL IMPLICATIONS OF COURNOT ON PRICING IN A MARKET WITH ADDITIONAL ENTRANTS



BCG finds that, “The Cournot model, in particular, provides an approach to estimating the impact on the average price of a product as more competing products enter the market. While there are some limitations on its applicability to drug markets, the model, along with the academic literature points in the same general direction, and does provide some evidence that more drugs could lead to lower net prices within the United States and, by implication, that OECD cost controls are imposing higher costs on U.S. patients.⁵⁹

In summary, from the perspective of U.S. consumers, foreign government price and access controls have likely had two notable effects: access to fewer new drugs and higher prices. Clearly both of these serious negative consequences highlight the importance of avoiding the imposition of such market intervention measures in the United States and the importance of aggressive U.S. Government efforts to convince counterparts overseas to adopt market-based reforms.

2. Effects on Patients Abroad

These price control and cost-containment mechanisms are also harmful to patients outside the United States, including in the countries in which they are imposed. Besides losing out on many new drugs, patients around the world suffer from delay in the launch of new products, lower utilization of the most innovative products and poorer health outcomes as a consequence.

⁵⁹ Annex D: BCG White Paper, “Adverse Consequences of OECD Government Interventions in Pharmaceutical Markets on the U.S. Economy and Consumer.”

A sizable economic literature exists that examines the effect of price controls on patient care. In his attached review of the literature at Annex C, Professor Kessler of Stanford University found that foreign price controls have had a substantial negative effect on the cost and quality of patient care. This negative effect on patient care occurs through two channels. First, as described above, price controls depress R&D and the discovery of new drugs. Second, price regulation delays drug launches, distorts consumers' choices toward less innovative drugs, and in some cases actually leads to increases in prices. Under these circumstances, it is no wonder then that a February 2003 article in *Business Week* stated that, "As a result of price controls, European consumers are heading toward second-class citizenship when it comes to access to medicine."⁶⁰

As already addressed in this Submission, foreign price and access controls result in substantial delays in the launch of new medicines. Such delays result both directly from government price regulatory procedures and from the incentives that such mechanisms impose on businesses to delay launches in low price countries to prevent the spillover distortions in freer markets (for example through reference pricing in third markets).

Moreover, even after a drug is launched, data indicate that foreign government price control measures lead to less diffusion of new medicines compared to the United States. The combined effect of all of the hurdles erected by foreign governments – whether they be strict doctor budgets, restrictive listings of new products on government formularies or tight volume controls on sales of new drugs – is a slower and diminished uptake of newer products.

BCG worked to quantify these combined effects in certain important therapeutic drug classes. The BCG analysis examined four classes of medicines and found that for all four classes, launches were delayed for innovative drugs in the OECD relative to the U.S. launch. These delays ranged from 13 months for statins to 24 months for anti-depressants. The BCG analysis also found that, even after medicines are launched, OECD countries lag the U.S. in terms of lower penetration rates for innovative medicines in classes such as diabetes, anti-depressants, statins, and anti-psychotics.⁶¹

Patients in price controlled OECD countries have access to older medicines while patients in the United States have access to newer, innovative medicines. For example, the BCG study found, "...the weighted average age of diabetes drugs in the United States is 5 years, as against 7-8 years in Canada, Germany and the United Kingdom, and as much as 19-23 years in France and Poland. As for anti-psychotics, U.S. patients are treated with drugs that are on average 8 years old, while patients in most of the other sample OECD countries receive drugs that are on average 18-21 years old."⁶²

⁶⁰ K. Capell, "Europe Pays a High Price for Cheap Drugs," *Business Week* (17 February 2003).

⁶¹ See Exhibit 6 in Annex D, "Delayed Use of Innovative Drugs in OECD."

⁶² Annex D: BCG White Paper, "Adverse Consequences of OECD Government Interventions in Pharmaceutical Markets on the U.S. Economy and Consumer." Note that Canada and the United Kingdom are exceptions, with drugs that are 11 and 10 years old on average. Exhibit 9 in Annex D, "Older Drugs Used to Treat Diseases in OECD."

Other important studies appear in the literature. A 2002 survey entitled, "Diffusion of Medicines in Europe," found shortfalls in the diffusion of state-of-the-art medicines between European countries for 20 key diseases. The study noted that the shortfalls in diffusion of new medicines resulted in large part from price containment measures.⁶³ The study revealed that although effective medicines do exist, not everyone in Europe is receiving adequate treatment. In some cases, patients are not treated at all and in other cases they receive outdated medicines (with lower effectiveness or with more severe side-effects), while prescribed dosages can also be too low to have an effect. Specific examples of the impact of price controls on patient access follow:

- **Cardiovascular Disease** - In Germany, 87 percent of all patients with coronary heart disease were not provided with modern lipid-lowering drugs (statins). In Italy, 83 percent of eligible patients did not receive statins.
- **Multiple Sclerosis** - In France, "less than 50 percent of patients [with Multiple Sclerosis] eligible for treatment with beta interferons actually receive it (only 10,000 from about 25,000 to 30,000)."
- **Schizophrenia** - In France it is estimated that there are 4.4 schizophrenia sufferers for every 1,000 people aged between 31 and 50 years, but only 2.4 people for every 1,000 are treated. For the treated patients the level of the use of innovative second generation drugs continues to be at a very low level.
- **Depression** - "The European average shows that only 18 percent of patients with severe depression received treatment with antidepressants." In Germany, of the percent of patients treated with antidepressants, "only one in three received an up-to-date treatment with modern antidepressants (SSRIs). The other 8 percent are treated with older substances with more side effects or less effective drugs like herbal preparations." In France, "recent studies have shown that 50 to 70 percent of patients with symptomatic depression are not treated at all, either with interpersonal or behavioural psychotherapies nor with antidepressant medication or a combination of both."⁶⁴

As noted, the BCG analysis demonstrated that on average, Americans are treated with newer more innovative medicines as compared to patients in a sample of OECD countries. Other studies have also confirmed that price and access controls tend to increase the use of older medicines. A recent study by IMS Consulting examined data from the U.S. and Europe, the two largest biotech markets, over the last ten years, and found that American patients have benefited through the introduction of more biotech medicines, and these medicines have been on the market for longer periods of time. The

⁶³ O. Schöffski, "Diffusion of Medicines in Europe," Prepared for the European Federation of Pharmaceutical Industries and Associations (EFPIA) (September 2002).

⁶⁴ Ibid.

report also noted that not only do Americans have access to a greater number of biotech medicines than Europeans, they also tend to use relatively newer products.⁶⁵

Similarly, a December 2002 report from the U.S. International Trade Commission examined pricing of prescription drugs and found that when a drug is widely available in the market the “effect of the cost-containment programs in some countries is the increased likelihood that older, lower cost products would be prescribed rather than newer, more innovative products.”⁶⁶

Price controls also have an impact on health outcomes for patients. For example, a study by Miller and Frech examined the effects of pharmaceuticals on disease mortality (taking into account obesity, tobacco use, and alcohol consumption) in 18 OECD countries in 2000.⁶⁷ The authors found pharmaceuticals play an important role in treating disease and increasing life expectancy. Another study by The Lewin Group found that many lives could be saved (and cost savings as well) if all eligible patients received statins.⁶⁸

All of these studies demonstrate the important negative effect of short-term cost-containment strategies on patient health. Not only do foreign government price and access controls hurt American patients, they do not even benefit the very populations that they are arguably trying to support.

C. Foreign Price Controls Hurt National Economies and Can Actually Increase Health Care Costs

Given that the imposition of government price controls on innovative pharmaceuticals has such significant negative ramifications for the quality of medical care abroad, one would hope that such measures at least serve their intended purpose of saving governments money. In fact, the opposite is true. By introducing these distortions into their national marketplace, recent evidence demonstrates that foreign governments actually incur substantial economic losses and higher costs elsewhere in their health care system. Even more importantly to U.S. policymakers, such measures impose additional costs on the U.S. economy even beyond the negative effects of patient care identified in the preceding section.

⁶⁵ IMS Health, “U.S. Outpaces Europe in Growth of Emerging Biotech Market: Industry Prospective” (17 January 2003).

⁶⁶ U.S. International Trade Commission, “Pricing of Prescription Drugs,” (Washington, D.C.: U.S. International Trade Commission, December 2000): Publication 3333.

⁶⁷ Miller and Frech, “Productivity of Health Care and Pharmaceuticals: Quality of Life, Cause of Death and the Role of Obesity” July 24, 2002 (draft).

⁶⁸ The Lewin Group, “Diffusion of Treatments Study: Statin Use for Hypercholesterolemia, Cross-Country Report” (2000).

1. Economic Consequences for the United States: Higher Costs, Fewer Jobs, Lower Exports

As described above, the effect of foreign price and access controls on the pharmaceutical industry is to depress its investment in R&D which means fewer life-saving and life-enhancing medicines are brought to market. In addition, U.S. prices may be higher because of the absence of these new drugs that would help increase market competition thereby driving down prices in many therapeutic classes of medicines. Beyond these effects, however, foreign price and access controls also have a significant impact on the U.S. economy through reduced exports, reduced jobs and direct harm to the U.S. pharmaceutical industry and its American shareholders.

The pharmaceutical industry is a key component of America's high tech economy. The pharmaceutical sector contributed \$229.2 billion in sales, \$75.4 billion in labor income, and nearly 1.1 million employees to the U.S. economy in 1999 alone.⁶⁹ The average wage in the industry is over \$18 per hour. The industry is among the top U.S. exporting industries, and ranks with the semiconductor, aerospace and computer industry in the value of its exports.

BCG's analysis found that price controls in OECD markets cost U.S. biopharmaceutical manufacturers 35-45 percent in terms of lost incremental revenues. Approximately 35,000 to 50,000 new incremental biopharmaceutical jobs would be created as a result in the United States. 20,000 to 30,000 of these new jobs would be R&D jobs which require a highly specialized skill set and are especially high-paying and valuable to the economy. To provide a sense of magnitude, the additions of these jobs reflects the addition of an area equivalent to one entirely new biotech cluster in the United States, such as Boston, Massachusetts biotech concentration.⁷⁰ By incorporating a multiplier effect,⁷¹ BCG estimates a total potential of 90,000 to 105,000 new jobs created as a result of eliminating cost controls in OECD countries. The generation of approximately 100,000 new jobs as a result of price controls in OECD countries being lifted, would be a positive addition to the U.S. job market and economy.

2. Economic Consequences for Europe: Decline of European Industry, Broad Economic Losses and Higher Health Care Costs, Scientific Brain Drain

The economic consequences for foreign governments of imposing these price and access controls are even more strikingly negative. They have resulted in a scientific brain drain in Europe, the relative decline of the European pharmaceutical industry and

⁶⁹ 1999 IMPLAN reports, PhRMA Annual Membership Survey, AD Little Analysis 2002.

⁷⁰ See BCG White Paper Exhibit 26 in Annex D, "The Number of New Jobs Added Would be the Equivalent to Adding One New Life Science Cluster."

⁷¹ A multiplier is a measure of the multiple effects produced by a given economic activity. It measures the so-called "ripple effects" that the pharmaceutical industry has on other industries and therefore the economy as a whole). Therefore, the types of jobs quantified by the multiplier include occupations ranging from construction workers that build a new pharmaceutical plant to a small business owner, who may count pharmaceutical companies as their primary customers.

distorted health care systems in Europe toward less cost-effective (but locally represented) health care products and services. These results suggest that the conventional wisdom that underlies part of the free-rider debate - Europe profits, while the United States pays - is wrong. The social and economic costs to Europe, in the form of delayed access to drugs, poorer health outcomes, lowered investment in research capabilities and a drain placed on high value pharmaceutical jobs, make the free-rider strategy a costly one to follow.

a. Government Price Controls Have Led to the Relative Decline of the Pharmaceutical Industry in Europe

Over the past decade, as OECD countries introduced additional price and access control mechanisms, the pharmaceutical industry in these countries outside the United States has stagnated while the U.S. pharmaceutical industry has grown.

Over the past 10 years, R&D investments have increased significantly in the United States, at about twice the rate of R&D growth in Europe. During the 1990s, the United States surpassed Europe as the leading site for pharmaceutical R&D. According to the European Federation of Pharmaceutical Industries and Associations (EFPIA), “The European pharmaceutical industry is losing competitiveness as compared to the U.S. industry and there is a process of concentration of R&D into North America.”⁷² In 1999, European pharmaceutical companies spent only 59 percent of their worldwide R&D in the EU, down from 73 percent in 1990. The United States was the main beneficiary of this shift in R&D expenditures.⁷³

Moreover, over the past several years, European pharmaceutical companies have begun to depart Europe and head to the United States. There are several reasons why there has been a transfer of research and facilities from Europe to the United States, including the science and technology base in the United States compared to Europe, as well as the public-private research partnerships that exist in the United States. However, one of the primary reasons for the transfer of research and facilities is price control policies and other cost-containment measures that have led to a lack of competitiveness in Europe as compared to the United States.

- May 2002, Novartis, a Swiss pharmaceuticals company, announced it was moving its company's research operations to Boston, Massachusetts. This represented a \$250 million investment in a new lab for 400 scientists on the Cambridge campus of MIT. According to Chris Viehbacher, president of GlaxoSmithKline in Europe, “Novartis’ move is a sign that the lack of competitiveness in Europe is actually accelerating...Other companies are bound to follow.”⁷⁴

⁷² European Federation of Pharmaceutical Industries and Associations, *Pharmaceutical Industry Chartbook* (Brussels, Belgium: EFPIA, 2001).

⁷³ *Ibid.*

⁷⁴ Daniel Domby and Victoria Griffith, “Pharmaceuticals Abandon Europe,” *Financial Times*, May 8, 2002.

- While GlaxoSmithKline still has its official headquarters in the U.K., its chief executive and head of research are now based in Philadelphia.
- Aventis, the Franco-German group, now manages its research from New Jersey.
- Pharmacia was a Swedish-based company until it merged with Upjohn in the mid-1990s. As part of the compromise with the Upjohn merger, the headquarters were initially based in the UK, but they were later shifted to New Jersey and merged with Monsanto. They subsequently decided to wind up their Swedish R&D operations altogether. Pharmacia has since merged with Pfizer, a U.S.-based company.
- In 2003, Boehringer Ingelheim moved its cardiovascular research from Biberach, Germany to the United States. The company has stated it plans to spend \$400 million to \$500 million to expand facilities in Connecticut. The project is expected to create 500 to 700 new jobs in the next six years. The expansion includes new labs to support R&D in the immunological, inflammatory and cardiovascular areas as well as support functions for medical and administrative organizations. According to Alessandro Banchi, board of managing directors, Boehringer Ingelheim, "This expansion marks a decisive step in the future of Boehringer Ingelheim in the United States."⁷⁵

A report issued in November 2000 by the Directorate General Enterprise of the European Commission studied the global competitiveness in pharmaceuticals from a European perspective, where price control programs have been in effect for years, and found that national regulation of prices in many EU markets has restricted competition. In its findings, the authors state that "the relative position of the US as a locus of innovation in pharmaceuticals has increased over the past decade compared to Europe."⁷⁶ The report credits the U.S. as the industry of "new drug research tool producers." In addition, according to analysts at SG Cowen, "Major drug companies are being left with little choice but to cut investments and manage the business to maintain returns. This means reduced R&D and fewer new drugs in Europe than in the USA."⁷⁷

These costs of imposing stringent pharmaceutical price and access controls in Europe are reflected in the numbers:

- Less drug innovation - there were 81 new molecular entities (NMEs) launched in Europe between 1993 and 1997 yet only 44 NMEs were launched between 1998 and 2002. Conversely, 48 NMEs were launched in the US between 1993 and

⁷⁵ "Boehringer Ingelheim Relocates, Expands," *Med Ad News*, November 2003.

⁷⁶ Pammolli F., et al., "Global Competitiveness in Pharmaceuticals: A European Perspective," Prepared for the Directorate General Enterprise of the European Commission," November 2000, p.7.

⁷⁷ *Ibid*

1997 and while 85 NMEs were launched between 1998 and 2002 - a 77% increase over the base period.

- Fewer high value-added jobs - the U.S. created 42% more high value-added pharmaceutical jobs than Europe from 1990 to 2001.
- Loss of corporate research centers - both U.S. and European R&D expenditures were approximately \$10 billion in 1992. From 1992 to 2002, U.S. pharmaceutical R&D expenditures grew by 11% (compounded annually) while European expenditures grew by just 8%, resulting in a substantial shift to the United States.⁷⁸

A similar situation has happened in Japan. The largest Japanese pharmaceutical company, Takeda, is only 15th largest in the world. The top Japanese companies lag behind in research. According to a Japan Pharmaceutical Manufacturers Association survey, the average annual level of R&D among the top 8 U.S. research-based companies in 2002 was \$2.6 billion; for the top 10 Japanese companies, it was \$450 million (*i.e.*, only 18% of the U.S. figure).⁷⁹

b. Government Price Controls Have Imposed Broader Costs on European Economies that Outweigh Any Short-Term Savings in Government Drug Budgets

In an attempt to address the total impact of the free-rider model on Europe, the consultancy group, Bain, recently presented a study that quantified the broader economic costs of price controls in Germany and compared those costs with the savings generated by the price controls.⁸⁰ The final “scorecard” was negative, and demonstrated that the short term savings gained from the imposition of price controls on pharmaceuticals are likely to be outweighed significantly by the associated economic losses caused by this intervention in the market.

The Bain analysis was based on 2002 data, and found the following:

- Pharmaceutical spending versus R&D investment - In 2002, Germany saved \$19 billion because it spent less per capita on pharmaceuticals than did the United States. In terms of R&D investment, however, Germany lost \$3 billion in 2002 as R&D investment in that country increased by 52% from 1992 to 2002, while

⁷⁸ JPMA Data Book, 2004. (U.S. Companies: Abbott, BMS, Lilly, J&J, Merck, Pfizer, Schering Plough, Wyeth. Japanese Companies: Takeda, Sankyo, Yamanouchi, Daiichi, Eisai, Fujisawa, Chagai, Shionogi, Taisho, Tanabe.)

⁷⁹ JPMA Data Book, 2004. (U.S. Companies: Abbott, BMS, Lilly, J&J, Merck, Pfizer, Schering Plough, Wyeth. Japanese Companies: Takeda, Sankyo, Yamanouchi, Daiichi, Eisai, Fujisawa, Chagai, Shionogi, Taisho, Tanabe.)

⁸⁰ Jim Gilbert & Paul Rosenberg, Bain & Company, Addressing the Innovation Divide: Imbalanced Innovation (January 22, 2004).

investment in the US increased by 184%. Lost patent values and "network effect" benefits equated to an additional \$1 billion in total R&D losses.

- High value-added jobs – The loss of such jobs cost Germany \$3 billion in lost wages in 2002. From 1990 to 2001, high value-added employees in Germany's pharmaceutical industry fell by 26% while the comparable figure in the United States increased by 52%. Additional losses related to having foregone these high value-added jobs, such as losses of tax revenues and other follow-on effects, totaled an additional \$5 billion.
- Corporate centers – In 2002, profits totaling \$3 billion in 2002 would have accrued if Germany's pharmaceutical industry had kept pace with its U.S. counterparts. In 1980, two German firms - Bayer and Hoechst - ranked among the world's top 10 pharmaceutical companies. Bayer has now fallen from the top-ten list, and Hoechst is no longer an independent company. Other related losses, such as taxes and corporate formation benefits, bring the aggregate loss from the shift in corporate centers to approximately \$5 billion.
- Health outcomes - Bain's analysis suggests that in 2002, Germany lost nearly \$5 billion from poorer health outcomes driven by less patient and physician access to the most innovative drugs, contributing to higher comparable hospitalization rates and absence rates from work.

Thus, when Germany's \$19 billion in savings from lower per capita pharmaceutical spending is offset by losses from reduced R&D investment and drug innovation, lost wages, vanishing corporate centers and poorer health outcomes - an approximate aggregate of \$22 billion - Germany's "net score" is actually a loss of \$3 billion in 2002. While this score will differ for other European countries depending on local conditions, it suggests that the free-rider model is not actually free for Europe and that European governments themselves should recognize their economic interest in moving toward more market-based health care regimes.

The cost savings associated with use of innovative pharmaceuticals have also been studied extensively by economist Frank Lichtenberg. In addition to imposing other costs throughout the economy, foreign price controls can actually increase health care costs for the governments that use them. Recent studies and reports have confirmed what many have assumed for years – pharmaceuticals often substitute for more costly hospital and physician care. A study in the September/October 2001 issue of *Health Affairs* by Frank R. Lichtenberg of Columbia University examined the association between the use of newer medicines and morbidity, mortality, and health spending. Lichtenberg found that patients using newer drugs were significantly less likely to die and lose workdays than those using older drugs. He also found that the use of newer medicines increased drug costs by \$18, but reduced hospital and other non-drug costs by \$129,⁸¹ meaning that for each additional \$1 spent on newer pharmaceuticals, \$6.17 is saved in total health care

⁸¹ F. Lichtenberg, "Benefits and Costs of Newer Drugs: An Update," National Bureau of Economic Research (June 2002).

spending. This is powerful evidence that new drugs not only save lives – they save money by reducing the need for other, more expensive treatments such as hospitalizations, emergency-room visits, and nursing-home care. This analysis suggests that focusing narrowly on cost-savings in the procurement of innovative pharmaceuticals is a counter-productive strategy even for policymakers whose primary goal is to save money on health care expenses.

c. Price Controls in Europe Have Fostered Inefficient Pharmaceutical Spending on High-Cost Generics

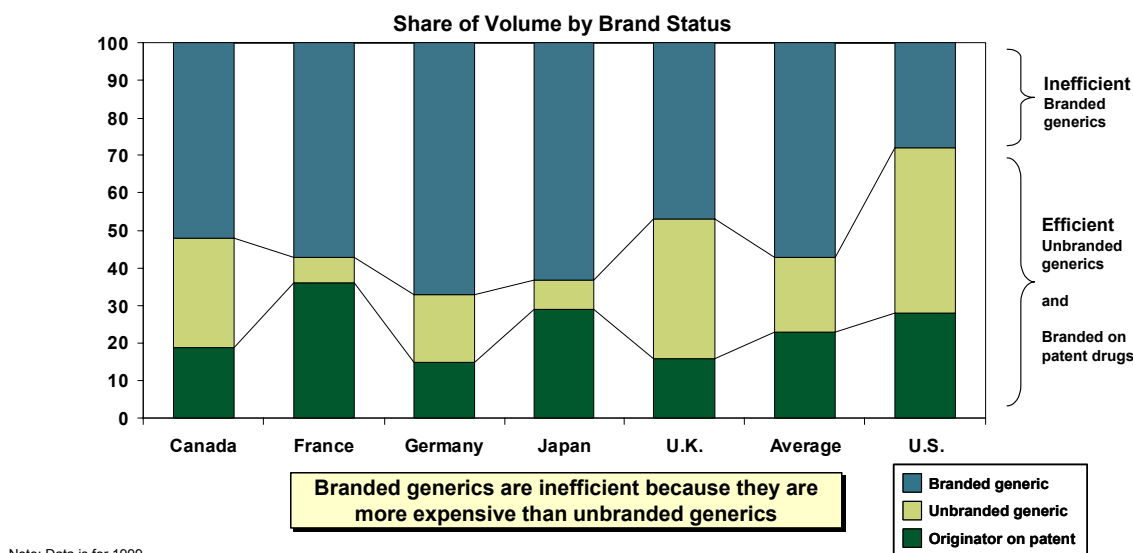
Government price and access controls on pharmaceuticals also skew the pattern of consumption of generic drugs in an inefficient manner. Because prescription drug prices are often lower in Europe and Japan, there is little incentive for generic manufacturers to enter those markets and compete aggressively on the basis of price. The result is that governments end up paying higher prices than needed for older, off-patent medicines. It is telling that, in general, generic use tends to be highest in countries with more market-oriented pharmaceutical sectors and lowest in countries where government bureaucrats intervene directly and with a heavy hand.

In their 2003 article entitled “*Prices and Availability of Pharmaceuticals: Evidence from Nine Countries*,” Danzon and Furukawa found that the level of generic drug use relative to total prescription volume is low in the price-regulated markets of France (28%) and Italy (34%), and higher in countries with freer pricing such as the U.S. (58%), Germany (61%) and the UK (49%).⁸² “Within the generic sector,” the authors write, “branded generics compete partly on brand image, whereas unbranded generics compete primarily on price. Thus, in the United States, where the generic sector is dominated by unbranded products, total generic share is 58% of units but only 18% of sales, reflecting relatively low generic prices. By contrast, in Germany, where most generics are branded, generic share is 61% of units but 34% of sales, reflecting relatively higher generic prices.”

Exhibit 13, from the Boston Consulting Group study, illustrates the large share of branded generic use in a handful of OECD countries compared to use in the United States. This figure demonstrates that the United States uses far fewer branded generic medicines than counterparts in Canada, France, Germany, Japan, and the United Kingdom.

⁸² Danzon and Furukawa, *Prices and Availability of Pharmaceuticals*, Health Affairs (2003).

HIGHER SHARE OF BRANDED GENERICS MAKES OECD DRUG SPEND LESS EFFICIENT THAN IN U.S.



Note: Data is for 1999

Source: BCG analysis of data in Danzon (2003), Health Affairs, pp W3-525 – original from calculations from IMS Health Midas data set 1999

One of the key findings from the BCG analysis is that, “...if the OECD countries were to shift their usage of pure generics to match U.S. promotions, we estimate that their health care systems could save as much as 20 percent of their annual overall drug spend. These resources could be reallocated to provide consumers greater access to more innovative drugs – and their accompanying health benefits – without any budget compromise.”⁸³ The BCG analysis clearly demonstrates that OECD countries may be squandering health care resources that could be more efficiently spent if not for the use of branded generic medicines in these markets.

Canada is an interesting case in point of this wasteful generic spending. While generic pharmaceutical prices in Canada are among the lowest in the OECD, a 2003 FDA White Paper found that generic prices for major drug categories in the United States are significantly lower than those found in Canada.⁸⁴ For six of seven important generic drugs (alprazolam, clonazepam, enalapril, fluoxetine, lisinopril, metformin, and metoprolol), the U.S. generic was priced less than the brand name versions in Canada. The price of the brand name version of enalapril in Canada was more than 5 times the price of the generic equivalent in the United States. These seven drugs represent the

⁸³ July 1, 2004 BCG White Paper, “Adverse Consequences of OECD Government Interventions in Pharmaceutical Markets on the U.S. Economy and Consumer.” See also Exhibit 15 in Annex D, “Mirroring U.S. Approach Would Free Up ~20% of Drug Spend for Other Applications.”

⁸⁴ U.S. Food and Drug Administration, *Generic Drug Prices in the U.S. are Lower than Drug Prices in Canada* (Rockville, MD: FDA, November 2003), available at <http://www.fda.gov/oc/whitepapers/drugprices.html>.

biggest selling chronic-use drugs for which first U.S. generic entry occurred in the last ten years.

In addition, all Canadian provinces except Quebec have mandatory generic substitution which erodes the innovator's market overnight when patents expire. The province of Ontario allows the first generic to come to market to charge 70% of the innovator product price and the second entrant is forced to go down to 63% of the innovator's price. This *de facto* kills any competitive incentive in the generic market place, leaving prices artificially high.

In contrast, in the United States generic versions of branded medicines become available as soon as a drug goes off patent, often for as little as 10% of the price, according to European pharmaceuticals analyst Kevin Scotcher at SG Cowen Securities Corporation in London.⁸⁵ European governments could save more money and improve access to new medicines by promoting the use of pure generics. Marc Booty, European pharmaceuticals analyst at Commerzbank Securities in London argues that the additional money could then be reinvested into more innovative drugs.⁸⁶

d. Price Controls Have Resulted in a Scientific Brain-Drain in Europe

In addition to the decline of the domestic innovative industry, the loss of R&D and the misallocation of health care resources, price controls in Europe and other developed markets are responsible for a notable scientific brain drain in favor of the United States in recent years. A recent article in *Time Europe* examined the reasons why scientists are "leaving in droves" for the United States and how Europe is trying to lure them back.⁸⁷ The article found that all over the United States, research facilities are full of bright, young Europeans that have been lured to America by generous funding, better facilities and a meritocratic culture. According to the article, in 2000, the United States spent £287 billion on R&D, £121 billion more than the EU. It should be no surprise then, according to the article, that the United States has 78% more high-tech patents per capita than Europe, which is especially weak in the IT and biotech sectors.

Just three years ago, EU leaders vowed to make the EU "the most competitive and dynamic knowledge-based economy in the world" by 2010. However, one of the signs of their failure is the continued drain of Europe's best and brightest scientific brains, who finish their degrees and pursue careers in the U.S. Some 400,000 European science and technology graduates now live in the United States. A survey released in November 2003 found that only 13% of European science professionals working abroad intended to return home to Europe.⁸⁸

⁸⁵ K. Capell, op. cit.

⁸⁶ Ibid.

⁸⁷ Jeff Chu, "How to Plug Europe's Brain Drain," *Time Europe*, 19 January 2004, vol. 163. no. 3.

⁸⁸ Ibid.

Brain drain is not a purely academic problem. According to the article, “Billions of euros and tens of thousands of jobs are at stake, because science drives economic growth in the IT, biotech and pharmaceutical sectors.” Andrew Wychkoff, an analyst with the OECD said, “Growth in the future will come from industries that are science based,” and Europe “needs scientists to irrigate them.”⁸⁹

e. European and Japanese Policymakers Have Recognized Social and Economic Harms Caused by their Pharmaceutical Price Control Policies

European academics and officials have candidly recognized the many heavy costs that intervention in the pharmaceutical market imposes on their economies. In a 2001 Report commissioned by the European Commission, entitled, “Global competitiveness in pharmaceuticals: A European perspective,” Alfonso Gambardella, Luigi Orsenigo, Fabio Pammolli looked at this phenomenon from a European perspective. The report examines the competitive position of the European pharmaceutical companies and industries, and compares them with the pharmaceutical companies and industries in other parts of the world, particularly the United States. The main finding of the report is that the European industry has indeed been losing competitiveness as compared to the United States. As a whole, Europe is lagging behind in its ability to generate, organize, and sustain innovation processes that are increasingly expensive and complex.

In March 2001, EU Enterprise Commissioner Erkki Liikanen and Public Health Commissioner David Byrne launched the so-called 'Group of ten' or 'G10' process involving top decision-makers in the EU on medicines. The aim of the G10 was to discuss a new agenda to improve the framework for competitiveness in the pharmaceutical industry and to harness its power to deliver on Europe's health care goals. Representatives of national governments, industry and patients were directly involved in this discussion. The high-level group delivered its recommendations in May 2002, and broadly supported the need for greater competition in national pricing and reimbursement systems.

Japan has similarly begun to recognize that its lack of reward for innovation has had an adverse affect on the establishment of a globally competitive life sciences industry. In 2002, the relative decline of the Japanese industry and its falling R&D situation prompted the Ministry of Health, Labor and Welfare (MHLW) in Japan to issue a new “Vision for the Pharmaceutical Industry.”⁹⁰ The Vision makes clear that its chief goal is: “To establish Japan's market as an attractive drug discovery environment in which global firms, whether domestic- or foreign-capital, can compete to develop, manufacture and market drugs - Japan's market must intrinsically be globally competitive.”⁹¹ Among other things, the Vision recognizes that one key to making

⁸⁹ Ibid.

⁹⁰ Government of Japan Ministry of Health, Labor and Welfare, “Toward Reinforcing the Global Competitiveness of the Pharmaceutical Industry, Mainstay of the ‘Century of Life’”, (April 2002).

⁹¹ Ibid.

Japan's industry more competitive is reforming the reimbursement system to make it more pro-innovation.

VI. Industry's Response

In light of the serious negative consequences of foreign government price and access controls on pharmaceutical products, PhRMA member companies have utilized a host of legal tools designed to eliminate or minimize the negative impacts of price controls or other market access barriers in markets abroad. In several instances, PhRMA member companies have challenged these practices in order to promote competition in the pharmaceutical market, instill greater transparency in government regulations, or to improve patient access to and choice of medical treatments.

PhRMA member companies have been particularly active in challenging ill-conceived price control policies in the European Union. We have done this through direct engagement with OECD member governments and through legal challenges to unlawful price controls in both the national and EU-level court systems.

In Europe, the principal legal grounds for challenge available to PhRMA member companies are the Treaty establishing the European Union⁹² and Community Directive 89/105, which sets forth Member State requirements when imposing pricing and reimbursement measures including:

- 180 days for determining pricing/reimbursement;
- decisions which are supported by “objective and verifiable criteria”;
- legal remedies for review of adverse decisions.

The text box below summarizes some recent industry activities on this point. These actions have produced some successes, but ultimately are limited in their potential to serve as catalysts for major change. Price control policies that disproportionately affect innovative products continue to be supported by national governments and tolerated by European authorities. Legal procedures to challenge Member state price/reimbursement controls are lengthy and resource-intensive. And even with successful rulings, Member states are not swift to comply or implement decisions. In many cases, Member states simply seek alternative means of imposing the price/reimbursement controls.

⁹² The Treaty provides:

- Article 3a – Member State and Community activities are to be “conducted in accordance with the principle of an open market economy with free competition.”
- Article 10 – Member States are prohibited from imposing measures that are contrary to Treaty objectives
- Article 28 – Member States are prohibited from imposing restrictions on imports or imposing other measures of “equivalent effect” (measures can include pricing/reimbursement controls)

**Select Examples of PhRMA
Industry Legal Challenges in
the European Union**

France

- Complaint filed with Commission in October 2000
 - French system of growth caps and penalties constituted

VII. Allowing Importation Would Import and Exacerbate the Negative Consequences of Foreign Price Controls to the United States

In light of these effects, the Administration and Congress should be vigilant in ensuring that foreign price controls are not imported into the United States by allowing the importation of pharmaceutical products from countries that artificially depress pharmaceutical prices at

below-market rates. Some have argued that legalizing importation of prescription drugs from other countries is a way to use the free market to bring lower cost medicines to American consumers.

Economists and trade experts have, however, argued that importation would not further free market principles, but instead would amount to “importing” foreign government price control regimes. For example, John E. Calfee of AEI writes that “Congress should dismiss all possibility of these scenarios by rejecting the drug importation legislation. It should not fall into the trap of thinking that as long as controls over U.S. prices were introduced by the government of a foreign country we would still have a free market. We wouldn’t have a free market, and we wouldn’t get the benefits of one.”⁹³

Similarly, Doug Bandow, Senior Fellow at the CATO Institute, has stated, “Most important, however, reimportation, no less than attempting to equalize prices internationally by legislative fiat, would effectively apply foreign price controls on the American market. This is, in fact, the policy’s objective.”⁹⁴

In a *Wall Street Journal* editorial, James K. Glassman and John R. Lott, Jr. explained, “In effect, re-importation of drugs would import something else to the U.S.: price controls, where the lack of such practices is the oxygen that allows pharmaceutical research to thrive. Drug-price controls are pernicious. While controls on oil and other products tend to be short-lived, as voters eventually object to the resulting shortages, the effects of drug regulations are more difficult to observe since they mainly affect medicines that haven’t been invented yet.”⁹⁵

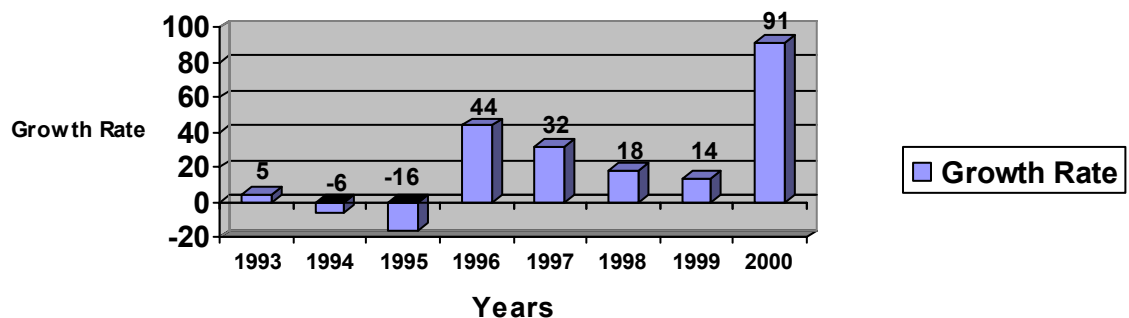
⁹³ J. Calfee, “The High Price of Cheap Drugs,” *The Weekly Standard*, 21 July 2003.

⁹⁴ D. Bandow, *Reimportation: Trojan Horse, Not Free Trade*, Institute for Policy Innovation (June 2003).

⁹⁵ J.K. Glassman and J.R. Lott, Jr., “The Drug World’s Easy Riders,” Commentary, *The Wall Street Journal*, 23 July 2003.

In light of the fact that importation is a mechanism to import foreign government price controls in the United States, it is important to understand the negative implications that even the threat of price controls has had in the United States. For example, during consideration of the Health Care Reform Act of 1993, various types of pharmaceutical price controls were proposed. While this legislation did not pass, the mere threat of price controls had a negative impact on the market value of many pharmaceutical firms.⁹⁶ Venture capital in biotechnology similarly dropped considerably in 1994 and 1995, reflecting concern about proposed government regulation of health care spending. An analysis by Arthur D. Little of the annual growth rate in biotech venture capital funding from 1993 to 2000 indicates declines of 6 and 16 percent in 1994 and 1995 respectively. Investment levels grew by 44 percent in 1996, when it was clear that then-President Clinton's plan would not be pursued.

Annual Growth of Biotechnology Venture Capital Financing (1993-2000)



Source: Ernst & Young 15th Annual Biotechnology Report, Arthur D. Little Analysis

A survey by the Gordon Public Policy Center of Brandeis University, conducted during the Clinton Health Care Reform debate, found that more than 70 percent of U.S. biotech firms feared that they would have to delay or curtail research because of the negative impact of health care reform on capital markets.⁹⁷ According to a survey conducted at that time by the trade association BIO, nearly 40 percent of biotech companies working to find treatments for HIV/AIDS, cancer, and diseases of the aging delayed or cancelled research because of capital shortfalls attributed to the health care reform debate.⁹⁸ Had the legislation actually passed, Professors Grabowski and Vernon

⁹⁶ See S. Ellison and W. Mullin, "Gradual Incorporation of Information: Pharmaceutical Stocks and the Evolution of President Clinton's Health Care Reform," *Journal of Law and Economics*, Vol. XLIV (April 2001).

⁹⁷ "BIO Airlifts Scientists, CEOs into D.C. for Lobbying Push," *Biotechnology Newswatch*, 1 August 1994.

⁹⁸ Ibid.

hypothesized that a substantial decline in R&D and innovative activity would have occurred.⁹⁹

Professor Frank Lichtenberg of Columbia University has argued that perception regarding future profits greatly influences current R&D spending and concludes, “policies that threaten to diminish future profits will reduce R&D investment today, even if they do not affect current profits.”¹⁰⁰

According to testimony before the Senate Committee on Health, Education, Labor and Pensions by Professor John Vernon, importation would have a significant effect on R&D, which in turn would impact life years.¹⁰¹ Vernon and his team of researchers did their analysis using results from recent studies on the growth rate of industry R&D (Scherer, 2001) and the cost of capital for pharmaceutical R&D (DiMasi, Hansen, and Grabowski, 2003; and Myers and Shyam-Sunder, 1996). They then calculated the present value of forgone R&D using standard methods. Finally, they combined this measure with estimates of the productivity of pharmaceutical R&D (Lichtenberg, 2002, 2003) to translate this policy-induced decline in R&D into human life years and lives, and then into dollars using standard estimates of the value of a human life year (Cutler and McClellan, 2001).

According to Vernon, “Our findings predict that a policy successfully reducing pharmaceutical prices (and profit margins) to the levels observed in markets where governments regulate drug prices will impose a cost of approximately 79 million life years, one million lives, or about \$8 trillion (Golec and Vernon, 2004). To place the later figure in context, consider that the 2003 GDP for the U.S. economy was roughly \$11 trillion. This cost estimate seems reasonable when compared to the recent findings by University of Chicago economists, Kevin Murphy and Robert Topel, that a permanent 10% reduction in the mortality from cancer and heart disease would be worth \$10 trillion dollars to Americans.

Joshua Boger, Chairman and CEO of Vertex, a biotech company, testified before a legislative panel in Massachusetts recently on the dangers of importation to the biotech community. According to Boger, “If price controls are [sic] imported successfully to the U.S., then Vertex and the rest of the adolescent biotech industry will simply and quite quickly vanish.”¹⁰²

An analysis by the Congressional Budget Office (CBO) of legislation that would allow importation of prescription medicines into the United States from 25

⁹⁹ H.G. Grabowski and J.M. Vernon, “Returns to R&D on New Drug Introductions in the 1980’s,” *Journal of Health Economics*, 13 (1994): 383-406.

¹⁰⁰ F.R. Lichtenberg, “Probing the Link Between Gross Profitability and R&D Spending,” *Health Affairs*, (September/October 2001): 221-222.

¹⁰¹ James Vernon, Ph.D, *Testimony Before the Senate Committee on Health, Education, Labor and Pensions* May 20, 2004).

¹⁰² C. Rowland, “Biotech Council Warns Against Drug Imports Bill Would Hurt Local Firms, State House Panel Told,” *The Boston Globe*, 9 April 2004.

countries estimated savings of just *1 percent* of total projected spending on drugs between 2004 and 2013. Savings to federal programs would be even lower, about one-half of one percent of federal spending on prescription drugs, according to the analysis. Finally, most of these projected savings will not even materialize for more than half a decade.¹⁰³

In sum, to expand the scope of foreign price controls through importation would greatly exacerbate all the negative ramifications of those controls detailed in this Submission without even saving the U.S. Government or consumers significantly on their pharmaceutical purchases.

VIII. Conclusion: Opposition to Foreign Market Access Barriers and Price Controls Should be a Core Element of U.S. Trade Policy

The pernicious effects of foreign government price and access controls hurt patients in the United States and abroad, hurt U.S. exports, cost good, high-quality U.S. jobs, and are not sound economic policy even for the countries that employ them. For all of these reasons, market-oriented reform of foreign pharmaceutical markets should be a top priority of U.S. trade policy.

International agreements and U.S. legislation both provide scope for trade action directed toward foreign price and access controls for pharmaceuticals. Although no existing trade agreement imposes comprehensive disciplines on trade distorting government price controls, the GATT has recognized the problematic nature of such government interventions since 1947. Article III:9 of that seminal trade agreement provides as follows:

The contracting parties recognize that internal maximum price control measures, even though conforming to the other provisions of this Article, can have effects prejudicial to the interests of contracting parties supplying imported products. Accordingly, contracting parties applying such measures shall take account of the interests of exporting contracting parties with a view to avoiding to the fullest practicable extent such prejudicial effects.

This text is evidence of countries' recognition that price controls can prejudice the trade interests of other countries and such prejudicial effects should be avoided. Over the past several years, the U.S. Government has also recognized the potential harm to U.S. trade interests as a result of certain countries' practices in this area. For example, in the U.S.-Japan Enhanced De-Regulation Initiative, initiated back in 1998, Japan committed to "recognize the valuation of innovation of pharmaceuticals" and "ensure transparency in the consideration of health care policies." *Birmingham Agreement (May 15, 1998)*. Bilateral efforts were also effective in improving the commercial environment in Korea during 1999-2001, when Korea agreed to list imported

¹⁰³ Congressional Budget Office, *Would Prescription Drug Importation Reduce U.S. Drug Spending* (Washington, D.C.: CBO, April 29, 2004).

medicines on its National Reimbursement List for the first time, and abandon a reference pricing scheme that would have disproportionately undermined the pricing of innovative medicines.

PhRMA welcomes recent steps taken by the Administration to begin to grapple with this complex set of issues in a more comprehensive fashion. The U.S.-Australia FTA, concluded earlier this year, represents an important step in the right direction. During the Australia negotiations, U.S. trade officials took the time to learn the intricacies of the Australian system and to understand the sometimes subtle manner in which that opaque system unfairly disadvantages the U.S. research-based pharmaceutical industry. While PhRMA is disappointed that not all market distortions and aspects of discrimination against innovative companies were resolved in the Agreement, we appreciate the important gains made in improving the transparency and fairness of the review process for new drugs in that country.

PhRMA also welcomes the recent creation of the position of an Assistant U.S. Trade Representative for Pharmaceutical Policy. We look forward to working with the Office of the U.S. Trade Representation, the Department of Commerce and other U.S. trade agencies in advancing U.S. trade policy interests and the interests of U.S. patients relating to foreign health care reform and global research and development.